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☐ 1. Document ID: US 6225450 B1

L7: Entry 1 of 52 File: USPT May 1, 2001

US-PAT-NO: 6225450
DOCUMENT-IDENTIFIER: US 6225450 B1

TITLE: DNA sequencing by mass spectrometry

DATE-ISSUED: May 1, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 536/22.1; 435/6, 536/118, 536/122, 536/24.3, 536/24.33, 536/26.13, 536/26.6, 536/28.52, 536/28.54, 536/28.55, 536/54

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6221583 B1

L7: Entry 2 of 52 File: USPT Apr 24, 2001

US-PAT-NO: 6221583
DOCUMENT-IDENTIFIER: US 6221583 B1

TITLE: Methods of detecting nucleic acids using electrodes

DATE-ISSUED: April 24, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
O'Connor; Stephen D.	Pasadena	CA	N/A	N/A
Gozin; Michael	Pasadena	CA	N/A	N/A
Yu; Changjun	Pasadena	CA	N/A	N/A
Meade; Thomas J.	Altadena	CA	N/A	N/A

US-CL-CURRENT: 435/6; 422/50, 422/68.1, 436/501

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6218118 B1

L7: Entry 3 of 52 File: USPT Apr 17, 2001

US-PAT-NO: 6218118
DOCUMENT-IDENTIFIER: US 6218118 B1

TITLE: Method and mixture reagents for analyzing the nucleotide sequence of nucleic acids by mass spectrometry

DATE-ISSUED: April 17, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sampson; Jeffrey R.	Burlingame	CA	N/A	N/A
Yakhini; Zohar H.	Palo Alto	CA	N/A	N/A
Webb; Peter G.	Menlo Park	CA	N/A	N/A
Sampas; Nicholas M.	San Jose	CA	N/A	N/A
Tsalenko; Anna M.	Chicago	IL	N/A	N/A
Myerson; Joel	Berkeley	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/173.1, 435/91.2, 435/91.5, 536/23.1, 536/24.31, 536/24.33, 536/25.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 4. Document ID: US 6214982 B1

L7: Entry 4 of 52 File: USPT Apr 10, 2001

US-PAT-NO: 6214982
DOCUMENT-IDENTIFIER: US 6214982 B1

TITLE: Ribonuclease resistant RNA preparation and utilization

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pasloske; Brittan L.	Austin	TX	78704	N/A
DuBois; Dwight	Austin	TX	78759	N/A
Brown; David	Austin	TX	78704	N/A
Winkler; Matthew	Austin	TX	78746	N/A

US-CL-CURRENT: 536/23.1; 530/350, 536/24.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 5. Document ID: US 6207370 B1

L7: Entry 5 of 52 File: USPT Mar 27, 2001

US-PAT-NO: 6207370
DOCUMENT-IDENTIFIER: US 6207370 B1

TITLE: Diagnostics based on mass spectrometric detection of translated target polypeptides

DATE-ISSUED: March 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Little; Daniel P.	La Jolla	CA	N/A	N/A
Higgins; Scott	Paisley	N/A	N/A	GBX
Koster; Hubert	La Jolla	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

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☐ 6. Document ID: US 6200761 B1

L7: Entry 6 of 52 File: USPT Mar 13, 2001

US-PAT-NO: 6200761
DOCUMENT-IDENTIFIER: US 6200761 B1

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: March 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	La Canada-Flintridge	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/287.1, 435/287.2, 536/22.1, 536/23.1, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

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☐ 7. Document ID: US 6194144 B1

L7: Entry 7 of 52 File: USPT Feb 27, 2001

US-PAT-NO: 6194144
DOCUMENT-IDENTIFIER: US 6194144 B1

TITLE: DNA sequencing by mass spectrometry

DATE-ISSUED: February 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	La Jolla	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.1, 436/173, 436/94

Inventor Search;

...completed examining records
S6 8 RD (unique items)
? t s6/3,ab/all

6/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12712944 BIOSIS NO.: 200000466446
Method of amplifying the signal of target nucleic acid sequence analyte.
AUTHOR: **Sampson Jeffrey R**(a); Dellinger Douglas J
AUTHOR ADDRESS: (a)Burlingame, CA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1233 (4):pNo pagination Apr. 25, 2000
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A method is disclosed of amplifying the signal of target nucleic acid sequence analyte using a rolling circle replication mechanism and a bidirectional primer. The repeating signal amplification sequence units contain tags which are directly or indirectly detectable. In addition, methods of capturing the tagged complementary nucleic acid sequence of the target nucleic acid sequence onto an array surface and detecting the captured target nucleic acid sequences are disclosed. Kits are also disclosed for enhancing detection of target nucleic acid sequences using a mechanism of rolling circle replication and a bidirectional primer to attach to the complementary nucleic acid sequence of the target nucleic acid sequence a large number of detectable tags.

2000

6/3,AB/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11398575 BIOSIS NO.: 199800179907
Evolution of a transfer RNA gene through a point mutation in the anticodon.
AUTHOR: Saks Margaret E(a); **Sampson Jeffrey R**; Abelson Joh
AUTHOR ADDRESS: (a)Dep. Biol., Univ. Oregon, Eugene, OR 97403**USA
JOURNAL: Science (Washington D C) 279 (5357):p1665-1670 March 13, 1998
ISSN: 0036-8075
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The transfer RNA (tRNA) multigene family comprises 20 amino acid-accepting groups, many of which contain isoacceptors. The addition of isoacceptors to the tRNA repertoire was critical to establishing the genetic code, yet the origin of isoacceptors remains largely unexplored. A model of tRNA evolution, termed "tRNA gene recruitment," was formulated. It proposes that a tRNA gene can be recruited from one isoaccepting group to another by a point mutation that concurrently changes tRNA amino acid identity and messenger RNA coupling capacity. A

test of the model showed that an Escherichia coli strain, in which the essential tRNAUGUThr gene was inactivated, was rendered viable when a tRNAArg with a point mutation that changed its anticodon from UCU to UGU (threonine) was expressed. Insertion of threonine at threonine codons by the "recruited" tRNAArg was corroborated by in vitro aminoacylation assays showing that its specificity had been changed from arginine to threonine. Therefore, the recruitment model may account for the evolution of some tRNA genes.

1998

6/3,AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10604389 BIOSIS NO.: 199699225534
An engineered Tetrahymena tRNA-Gln for in vivo incorporation of unnatural amino acids into proteins by nonsense suppression.
AUTHOR: Saks Margaret E; **Sampson Jeffrey R**; Nowek Mark W; Kearney Patrick C; Du Fangyong; Abelson John N; Lester Henry A; Dougherty Dennis A(a
AUTHOR ADDRESS: (a)Div. Chem. and Chem. Eng.-164-30, Calif. Inst. Technol., Pasadena, CA 91125**USA
JOURNAL: Journal of Biological Chemistry 271 (38):p23169-23175 1996
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A new tRNA, THG73, has been designed and evaluated as a vehicle for incorporating unnatural amino acids site-specifically into proteins expressed in vivo using the stop codon suppression technique. The construct is a modification of tRNA-Glu(CUA) from Tetrahymena thermophila, which naturally recognizes the stop codon UAG. Using electrophysiological studies of mutations at several sites of the nicotinic acetylcholine receptor, it is established that THG73 represents a major improvement over previous nonsense suppressors both in terms of efficiency and fidelity of unnatural amino acid incorporation. Compared with a previous tRNA used for in vivo suppression, THG73 is as much as 100-fold less likely to be acylated by endogenous synthetases of the Xenopus oocyte. This effectively eliminates a major concern of the in vivo suppression methodology, the undesirable incorporation of natural amino acids at the suppression site. In addition, THG73 is 4-10-fold more efficient at incorporating unnatural amino acids in the oocyte system. Taken together, these two advances should greatly expand the range of applicability of the in vivo nonsense suppression methodology.

1996

6/3,AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10439678 BIOSIS NO.: 199699060823
Variant minihelix RNAs reveal sequence-specific recognition of the helical tRNA-Ser acceptor stem by E. coli seryl-tRNA synthetase.
AUTHOR: Saks Margaret E; **Sampson Jeffrey R**
AUTHOR ADDRESS: Div. Biology, 147-74, Calif. Inst. Technol., Pasadena, CA 91125**USA
JOURNAL: EMBO (European Molecular Biology Organization) Journal 15 (11):p 2843-2849 1996
ISSN: 0261-4189
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Aminoacylation rate determinations for a series of variant RNA minihelix substrates revealed that Escherichia coli seryl-tRNA synthetase (SerRS) recognizes the 1-72 through 5-68 base pairs of the E. coli tRNA-Ser acceptor stem with the major recognition elements clustered between positions 2-71 and 4-69. The rank order of effects of canonical base pair substitutions at each position on k-cat/K-m was used to assess the involvement of major groove functional groups in recognition. Conclusions based on the biochemical data are largely consistent with the interactions revealed by the refined structure of the homologous Thermus thermophilus tRNA-Ser-SerRS complex that Cusack and colleagues report in the accompanying paper. Disruption of an end-on hydrophobic interaction between the major groove C5(H) of pyrimidine 69 and an aromatic side chain of SerRS is shown to significantly decrease k-cat/K-m of a minihelix substrate. This type of interaction provides a means by which proteins can recognize the binary information of 'degenerate' sequences, such as the purine-pyrimidine base pairs of tRNA-Ser. The 370 base pair is shown to contribute to recognition by SerRS even though it is not contacted specifically by the protein. The latter effect derives from the organization of the specific contacts that SerRS makes with the neighboring 2-71 and 4-69 acceptor stem base pairs.

1996

6/3,AB/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09857256 BIOSIS NO.: 199598312174
Evolution of tRNA recognition systems and tRNA gene sequences.
AUTHOR: Saks Margaret E(a); **Sampson Jeffrey R**
AUTHOR ADDRESS: (a)Div. Biol. 147-75, Calif. Inst. Technol., Pasadena, CA 91125**USA
JOURNAL: Journal of Molecular Evolution 40 (5):p509-518 1995
ISSN: 0022-2844
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The aminoacylation of tRNAs by the aminoacyl-tRNA synthetases recapitulates the genetic code by dictating the association between amino acids and tRNA anticodons. The sequences of tRNAs were analyzed to investigate the nature of primordial recognition systems and to make inferences about the evolution of tRNA gene sequences and the evolution of the genetic code. Evidence is presented that primordial synthetases recognized acceptor stem nucleotides prior to the establishment of the three major phylogenetic lineages. However, acceptor stem sequences probably did not achieve a level of sequence diversity sufficient to faithfully specify the anticodon assignments of all 20 amino acids. This putative bottleneck in the evolution of the genetic code may have been alleviated by the advent of anticodon recognition. A phylogenetic analysis of tRNA gene sequences from the deep Archaea revealed groups that are united by sequence motifs which are located within a region of the tRNA that is involved in determining its tertiary structure. An association between the third anticodon nucleotide (N36) and these sequence motifs suggests that a tRNA-like structure existed close to the time that amino acid-anticodon assignments were being established. The sequence analysis also revealed that tRNA genes may evolve by anticodon mutations that recruit tRNAs from one isoaccepting group to another. Thus tRNA gene evolution may not always be monophyletic with respect to each isoaccepting group.

1995

6/3,AB/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09823089 BIOSIS NO.: 199598278007
Nicotinic receptor binding site probed with unnatural amino acid incorporation in intact cells.
AUTHOR: Nowak Mark W; Kearney Patrick C; **Sampson Jeffrey R**; Saks Margaret E; Labarca Cesar G; Silverman Scott K; Zhong Wenge; Thorson Jon; Abelson John N; Davidson Norman; Schultz Peter G; Dougherty Dennis A; Lester Henry A(a
AUTHOR ADDRESS: (a)Div. Biol., California Inst. Technology, Pasadena, CA 91125**USA
JOURNAL: Science (Washington D C) 268 (5209):p439-442 1995
ISSN: 0036-8075
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The nonsense codon suppression method for unnatural amino acid incorporation has been applied to intact cells and combined with electrophysiological analysis to probe structure-function relations in the nicotinic acetylcholine receptor. Functional receptors were expressed in Xenopus oocytes when tyrosine and phenylalanine derivatives were incorporated at positions 93, 190, and 198 in the binding site of the alpha subunit. Subtle changes in the structure of an individual side chain produced readily detectable changes in the function of this large channel protein. At each position, distinct features of side chain structure dominated the dose-response relation, probably by governing the agonist-receptor binding.

1995

6/3,AB/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09114098 BIOSIS NO.: 199497122468
The transfer RNA identity problem: A search for rules.
AUTHOR: Saks Margaret E(a); **Sampson Jeffrey R**(a); Abelson John N
AUTHOR ADDRESS: (a)Div. Biol., Calif. Inst. Technol., Pasadena, CA 91125** USA
JOURNAL: Science (Washington D C) 263 (5144):p191-197 1994
ISSN: 0036-8075
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Correct recognition of transfer RNAs (tRNAs) by aminoacyl-tRNA synthetases is central to the maintenance of translational fidelity. The hypothesis that synthetases recognize anticodon nucleotides was proposed in 1964 and had considerable experimental support by the mid-1970s. Nevertheless, the idea was not widely accepted until relatively recently in part because the methodologies initially available for examining tRNA recognition proved hampering for adequately testing alternative hypotheses. Implementation of new technologies has led to a reasonably complete picture of how tRNAs are recognized. The anticodon is indeed important for 17 of the 20 Escherichia coli isoaccepting groups. For many of the isoaccepting groups, the acceptor stem or position 73 (or both) is important as well.

```
Set      Items   Description
S1        3859   RNA AND POLYMERAS? AND ANALOG? AND PY<2000
S2          30   S1 AND (2 (W) THIOCYTIDINE OR PYRROLOPYRIMIDINE OR INOSINE
               OR 2 (W)THIOTHYMIDINE OR 2 (W) AMINOADENOSIN OR 2 (W) THIOCYT-
               IDINE)
S3          27   RD (unique items)
S4        3829   S1 NOT S2
S5         334   S4 AND MUTANT?
S6           9   S5 AND POLYMERIZ?
S7           7   RD (unique items)
? s s4 and rna (w) polymerase
            3829  S4
          679253  RNA
          348274  POLYMERASE
           43838  RNA(W)POLYMERASE
      S8    1642  S4 AND RNA (W) POLYMERASE
? s s8 and analog
            1642  S8
           80622  ANALOG
      S9     290  S8 AND ANALOG
? rd
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...completed examining records
     S10     206  RD (unique items)
? t s10/3,ab/all

 10/3,AB/1      (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10231812   99292802   PMID: 10362544
  3-D organization of ribosomal transcription units after DRB inhibition of
**RNA polymerase** II transcription.
  Panse SL; Masson C; Heliot L; Chassery JM; Junera HR; Hernandez-Verdun D
  Institut Jacques Monod, 75251 Paris Cedex 05, France.
  Journal  of  cell  science (ENGLAND)  Jul **1999**,  112  (  Pt  13)
 p2145-54,  ISSN 0021-9533  Journal Code: HNK
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  In  each  bead  of  the  nucleolar necklace, using adenosine **analog**
DRB-treated PtK1 cells, we investigated the three components of rDNA
transcription, i.e. the gene, transcription factor UBF and transcripts. In
situ hybridization revealed the unraveling and 3-D dispersion of most of
the rDNA coding sequences within the nucleus. The signals were small, of
similar intensity and tandemly organized in the necklace. This observation
is compatible with the fact that they might correspond to single gene
units. Active transcription was visualized in these units, demonstrating
that they were active functional units. Transcript labeling was not similar
for each unit, contrary to UBF labeling. UBF and rRNA transcripts were only
partially colocalized, as demonstrated by 3-D image analysis and
quantification. As visualized by electron microscopy, the necklace was
composed of a small fibrillar center partially surrounded by a dense
fibrillar component. The 3-D arrangement of this individual unit in the
necklace, investigated both by confocal and electron microscopy in the same
cells, showed that the individual beads were linked by a dense fibrillar
component. The reversibility of this organization after removal of DRB
indicated that the beads in the necklace are certainly the elementary
functional domain of the nucleolus. In addition, these results lead us to
suggest  that  the  organization  of  a  functional  domain,  presumably
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corresponding to a single gene, can be studied by in situ approaches.

10/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10097923 99157100 PMID: 10037819
Oligonucleotide-europium complex conjugate designed to cleave the 5' cap structure of the ICAM-1 transcript potentiates antisense activity in cells.
Baker BF; Lot SS; Kringel J; Cheng-Flournoy S; Villiet P; Sasmor HM; Siwkowski AM; Chappell LL; Morrow JR
ISIS Pharmaceuticals Inc., 2292 Faraday Avenue, Carlsbad, CA 92009, USA and Department of Chemistry,State University of New York, Buffalo, NY 14260-3000, USA. bbaker@isisph.com
Nucleic acids research (ENGLAND) Mar 15 **1999**, 27 (6) p1547-51, ISSN 0305-1048 Journal Code: 08L
Contract/Grant No.: R44 AI30333, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The 5' cap structure of mRNA is a N7 methylated guanosine residue that is linked by a 5'-5' triphosphate linkage to the 5'-terminus of cellular and viral RNAs synthesized by **RNA polymerase** II. This unique structure facilitates several processes of mRNA metabolism, including splicing, nucleocytoplasmic transport,initiation of translation, and degradation. Previous research has demonstrated that the lanthanide macrocycle complex, Eu(THED)3+, effectively cleaves the 5' cap structure of mRNA in solution by nucleophilic attack of the triphosphate linkage via the metal-activated hydroxyethyl group of the THED ligand. This report shows that attachment of a Eu(THED)3+**analog** to the 3'-terminus of an antisense oligonucleotide, which targets the 5'-terminus of the intercellular adhesion molecule 1 mRNA, potentiates the inhibitory activity of the antisense oligonucleotide in cytokine-treatedendothelial cells.

10/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10090349 99141236 PMID: 9973628
Probing the environment of nascent **RNA** in Escherichia coli transcription elongation complexes utilizing a new fluorescent ribonucleotide **analog**.
Hanna MM; Yuriev E; Zhang J; Riggs DL
Department of Chemistry and Biochemistry, University of Oklahoma, 620 Parrington Oval Room 208, Norman, OK 73019-0370, USA. mhanna@chemdept.chem.ou.edu
Nucleic acids research (ENGLAND) Mar 1 **1999**, 27 (5) p1369-76, ISSN 0305-1048 Journal Code: 08L
Contract/Grant No.: RO1 GM47493, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We report the synthesis and characterization of 5-thioacetamidofluorescein-uridine 5'-triphosphate (5-SF-UTP), and its application to the characterization of the environment of the nascent **RNA** during trans-cription. This **analog** specifically replaced UTP as a transcription substrate for Escherichia coli and T7 **RNA polymerases**, and yeast **RNA polymerase** III. Escherichia coli transcription complexes containing **analog** incorporated at only position +21 of the **RNA** were prepared. The **RNA** was then elongated in the absence of **analog**, moving the fluorescent group further away from the enzyme active site, and the fluorescence polarization was measured. **Analog** positioned near the 3' end of the transcript exhibited significantly increased polarization relative to that of free

probe, consistent with the constrained environment of the **RNA** in the DNA-**RNA** hybrid. **Analog** positioned 14 nucleotides from the 3' end exhibited significantly decreased polarization relative to that at the 3' end of the **RNA**, but only slightly above that of free **RNA**, suggesting that the probe was on the solvent-exposed surface of the **polymerase**. Molecular modeling of these **analog**-substituted RNAs produced structures consistent with the experimental data. The excellent substrate properties of this **analog** make it useful for the characterization of the environment of **RNA** not only during transcription and translation, but in any type of ribonucleoprotein complex.

10/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10031048 99054866 PMID: 9835515
In vitro inhibition of hepadnavirus **polymerases** by the triphosphates of BMS-200475 and lobucavir.
Seifer M; Hamatake RK; Colonno RJ; Standring DN
Pharmaceutical Research Institute, Bristol-Myers Squibb, Wallingford, Connecticut 06492, USA.
Antimicrobial agents and chemotherapy (UNITED STATES) Dec **1998**, 42 (12) p3200-8, ISSN 0066-4804 Journal Code: 6HK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The guanosine **analogs** BMS-200475 and lobucavir have previously been shown to effectively suppress propagation of the human hepatitis B virus (HBV) and woodchuck hepatitis virus (WHV) in 2.2.15 liver cells and in the woodchuck animal model system, respectively. This repression was presumed to occur via inhibition of the viral **polymerase** (Pol) by the triphosphate (TP) forms of BMS-200475 and lobucavir which are both produced in mammalian cells. To determine the exact mode of action, BMS-200475-TP and lobucavir-TP, along with several other guanosine **analog**-TPs and lamivudine-TP were tested against the HBV, WHV, and duck hepatitis B virus (DHBV) **polymerases** in vitro. Estimates of the 50% inhibitory concentrations revealed that BMS-200475-TP and lobucavir-TP inhibited HBV, WHV, and DHBV Pol comparably and were superior to the other nucleoside-TPs tested. More importantly, both **analogs** blocked the three distinct phases of hepadnaviral replication: priming, reverse transcription, and DNA-dependent DNA synthesis. These data suggest that the modest potency of lobucavir in 2.2.15 cells may be the result of poor phosphorylation in vivo. Kinetic studies revealed that BMS-200475-TP and lobucavir-TP competitively inhibit HBV Pol and WHV Pol with respect to the natural dGTP substrate and that both drugs appear to bind to Pol with very high affinities. Endogenous sequencing reactions conducted in replicative HBV nucleocapsids suggested that BMS-200475-TP and lobucavir-TP are nonobligate chain terminators that stall Pol at sites that are distinct yet characteristically two to three residues downstream from dG incorporation sites.

10/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09858526 98337907 PMID: 9671810
Intracellular **RNA** cleavage by the hairpin ribozyme.
Seyhan AA; Amaral J; Burke JM
Markey Center for Molecular Genetics, Department of Microbiology and Molecular Genetics, 306 Stafford Hall, The University of Vermont, Burlington, VT 05405, USA.
Nucleic acids research (ENGLAND) Aug 1 **1998**, 26 (15) p3494-504 , ISSN 0305-1048 Journal Code: O8L

Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Studies involving ribozyme-directed inactivation of targeted **RNA** molecules have met with mixed success, making clear the importance of methods to measure and optimize ribozyme activity within cells. The interpretation of biochemical assays for determining ribozyme activity in the cellular environment have been complicated by recent results indicating that hammerhead and hairpin ribozymes can cleave **RNA** following cellular lysis. Here, we report the results of experiments in which the catalytic activity of hairpin ribozymes is monitored following expression in mammalian cells, and in which post-lysis cleavage is rigorously excluded through a series of biochemical and genetic controls. Following transient transfection, self-processing transcripts containing active and inactive hairpin ribozymes together with cleavable and non-cleavable substrates were generated within the cytoplasm of mouse OST7-1 cells using T7 **RNA polymerase**. Unprocessed **RNA** and products ofintracellular cleavage were detected and analyzed using a primer-extension assay. Ribozyme-containing transcripts accumulated to a level of 4 x 10(4) copies per cell, and self-processing proceeded to an extent of >75% within cells. Cellular **RNA** processing was blocked by mutations within the ribozyme (G8A, G21U) or substrate (DeltaA-1) that, in vitro , eliminate cleavage without affecting substrate binding. In addition to self-processing activity, trans -cleavage reactions were supported by the ribozyme-containing product of the self-processing reaction, and by the ribozyme linked to the non-cleavable substrate **analog**. Ribozyme activity was present in extracts of cells expressing constructs with active ribozyme domains. These results provide direct biochemical evidence for the catalytic activity of the hairpin ribozyme in a cellular environment, and indicate that self-processing ribozyme transcripts may be well suited for cellular **RNA**-inactivation experiments.

10/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09739518 98241249 PMID: 9582093

The chemical basis of adenosine conservation throughout the Tetrahymena ribozyme.

Ortoleva-Donnelly L; Szewczak AA; Gutell RR; Strobel SA
Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, Connecticut 06520, USA.

RNA (UNITED STATES) May **1998**, 4 (5) p498-519, ISSN 1355-8382
Journal Code: CHB
Contract/Grant No.: GM48207, GM, NIGMS; GM54839, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Adenosines are present at a disproportionately high frequency within several **RNA** structural motifs. To explore the importance of individual adenosine functional groups for group I intron activity, we performed Nucleotide **Analog** Interference Mapping (NAIM) with a collection of adenosine **analogues**. This paper reports the synthesis, transcriptional incorporation, and the observed interference pattern throughout the Tetrahymena group I intron for eight adenosine derivatives tagged with an alpha-phosphorothioate linkage for use in NAIM. All of the **analogues** were accurately incorporated into the transcript as an A. The sites that interfere with the 3'-exon ligation reaction of the Tetrahymena intron are coincident with the sites of phylogenetic conservation, yet the interference patterns for each **analogue** are different. These interference data provide several biochemical constraints that improve our understanding of the Tetrahymena ribozyme structure. For example, the data support an essential A-platform within the J6/6a region, major groove packing of the P3 and P7 helices, minor groove packing of the

P3 and J4/5 helices, and an axial model for binding of the guanosine cofactor. The data also identify several essential functional groups within a highly conserved single-stranded region in the core of the intron (J8/7). At four sites in the intron, interference was observed with 2'-fluoro A, but not with 2'-deoxy A. Based upon comparison with the P4-P6 crystal structure, this may provide a biochemical signature for nucleotide positions where the ribose sugar adopts an essential C2'-endo conformation. In other cases where there is interference with 2'-deoxy A, the presence or absence of 2'-fluoro A interference helps to establish whether the 2'-OH acts as a hydrogen bond donor or acceptor. Mapping of the Tetrahymena intron establishes a basis set of information that will allow these reagents to be used with confidence in systems that are less well understood.

10/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09591859 97456508 PMID: 9311822
A human primary T-lymphocyte-derived human immunodeficiency virus type 1 Tat-associated kinase phosphorylates the C-terminal domain of **RNA polymerase** II and induces CAK activity.
Nekhai S; Shukla RR; Kumar A
Department of Biochemistry and Molecular Biology, George Washington University School of Medicine, Washington, D.C. 20037, USA.
Journal of virology (UNITED STATES) Oct **1997**, 71 (10) p7436-41, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: CA72147, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Tat protein mediates transactivation of human immunodeficiency virus type 1 (HIV-1), which results in more-efficient transcript elongation. Since phosphorylation of C-terminal domain (CTD) of **RNA polymerase** II correlates with its enhanced processivity, we studied the properties of a Tat-associated CTD kinase derived from mitogenically stimulated human primary T lymphocytes (TTK). TTK binds to full-length Tat and specifically phosphorylates CTD and CDK2. This dual kinase activity is characteristic of CDK-activating kinase (CAK). The CTD kinase activity is induced upon mitogenic stimulation of primary T lymphocytes. Fractionation of T-cell lysate demonstrates that Tat-associated CTD kinase activity elutes in two peaks. About 60% of Tat-associated CTD kinase copurifies with CDK2 kinase activity and contains the CAK components CDK7 and cyclin H. The rest of Tat-associated kinase is free of CDK2 kinase activity and the CAK components and thus may represent a novel CTD kinase. The kinase activities of TTK are blocked by the adenosine **analog** 5,6-dichloro-1-beta-D-ribofuranosyl-benzimidazole (DRB) as well as by the kinase inhibitor H8 at concentrations known to block transcript elongation. Importantly, the Tat-associated kinase markedly induced CAK. We suggest that the mechanism of Tat-mediated processive transcription of the HIV-1 promoter includes a Tat-associated CAK activator.

10/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09532867 97473529 PMID: 9332383
An epitope tagged mammalian/prokaryotic expression vector with positive selection of cloned inserts.
Schneider S; Georgiev O; Buchert M; Adams MT; Moelling K; Hovens CM
Institut fur Medizinische Virologie, Universitat Zurich, Switzerland.
Gene (NETHERLANDS) Sep 15 **1997**, 197 (1-2) p337-41, ISSN 0378-1119 Journal Code: FOP
Languages: ENGLISH

Document type: Journal Article
Record type: Completed

A dual eukaryotic/prokaryotic expression vector has been developed which combines the features of positive selection for cloned inserts along with the production of an epitope-tagged cDNA insert by transient transfection in mammalian cells as well as high level induced expression in E. coli cells harbouring T7 **RNA polymerase**. This vector, pZilch, has two MCSs flanking a mutant E. coli phenylalanyl-tRNA synthetase gene, pheS, which when expressed in combination with the phenylalanine **analog** p-CI-Phe, results in termination of host cell protein synthesis. Cloning of inserts using unique sites in the flanking MCS regions results in loss of the pZilch pheS allele and hence permits growth of colonies harbouring recombinants on p-Cl-Phe plates. Additional features of the vector include an optimal Kozak consensus sequence for high level eukaryotic cell expression and an efficient prokaryotic translation initiation site in frame and downstream from the eukaryotic initiation site. Recombinant proteins can be produced with an N-terminal FLAG epitope which can be removed via a specific protease cleavage site. Flanking T7 and SP6 **RNA polymerase** promoter sites permit in vitro transcription and translation of cloned inserts. A derivative of the vector has also been constructed enabling nuclear accumulation of the tagged proteins via an SV40 nuclear localisation signal upstream of the 5' MCS.

10/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09519659 96399750 PMID: 8806182

Influenza A virus **RNA**-dependent **RNA polymerase** cleaves influenza mRNA in vitro.

Peng Q; Galarza JM; Shi L; Summers DF
Department of Microbiology and Molecular Genetics, and Medicine, University of California, Irvine 92717-4025, USA.

Virus research (NETHERLANDS) Jun **1996**, 42 (1-2) p149-58, ISSN 0168-1702 Journal Code: X98
Contract/Grant No.: AI 12316, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

We have investigated the endonuclease activity of the influenza A virus **RNA polymerase** in an in vitro assay with an artificial influenza-like mRNA containing a cap structure at its 5' terminus, followed by a 10 nt beta-globin mRNA sequence, and the 5' and 3' conserved termini of a truncated nucleoprotein (NP) cRNA influenza sequence. Results showed that partially purified virion ribonucleoprotein complexes (RNPs) and micrococcal nuclease treated RNPs cleaved the artificial influenza-like mRNA substrate specifically at positions near the 5' terminus to generate capped 14 and 15 nucleotide long **RNA** fragments which subsequently served as primers to initiate transcription. The endonuclease activity was completely blocked by addition of cap **analog** and competitively inhibited by added globin mRNA. Furthermore, an in vitro reconstituted influenza **RNA** transcription reaction containing a truncated NP vRNA as template, micrococcal nuclease treated RNPs and globin mRNA as primer, synthesized capped and uncapped full length (+) sense products. Enzyme kinetics showed that capped **RNA** was made earlier in the reaction; it reached a peak at 120 min and then declined. However, uncapped cRNA synthesis appeared later and remained as the dominant product later in the reaction. The nature of these products was confirmed by ribonuclease protection assays and by primer extension.

10/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09421026 97474271 PMID: 9335295
Transcriptional characterization of the Rickettsia prowazekii major macromolecular synthesis operon.
Shaw EI; Marks GL; Winkler HH; Wood DO
Department of Microbiology and Immunology, University of South Alabama College of Medicine, Mobile 36688, USA.
Journal of bacteriology (UNITED STATES) Oct **1997**, 179 (20) p6448-52, ISSN 0021-9193 Journal Code: HH3
Contract/Grant No.: AI20384, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Recent studies have demonstrated that Rickettsia prowazekii can regulate transcription of selected genes at the level of initiation. However, little information concerning the existence of operons and coordinate gene regulation in this obligate intracellular parasitic bacterium is available. To address these issues, we have focused on the rpoD gene linkage group (greA-open reading frame 23 [ORF23]-dnaG-rpoD), which includes the rickettsial **analog** (ORF23-dnaG-rpoD) of the major macromolecular synthesis operon (MMSO). The rickettsial MMSO consists of an ORF coding for a protein of unknown function the structural genes for DNA primase (dnaG) and the major sigma factor of **RNA polymerase** (rpoD). RNase protection assays (RPA) were used to determine if these genes are organized into an operon controlled by multiple promoters and the quantities of transcripts produced by these genes relative to each other. RPA with a probe spanning the 270-base greA-ORF23 intervening region identified a putative transcriptional promoter within the intervening sequence. Multiple RPA probes spanning the next 4,041 bases of the linkage group demonstrated the presence of a continuous transcript and thus the existence of an operon. A probe spanning the dnaG-rpoD region revealed that two additional mRNA fragments were also protected, which enabled us to identify additional putative promoters for rpoD within dnaG. Primer extension determined that the 5' ends of the three transcripts consist separately of adenine (located 227 bases upstream of ORF23) and uracil and adenine (located 336 and 250 bases upstream of rpoD, respectively). Quantitation of transcripts produced by the three ORFs determined the relative amounts of transcripts (ORF23 to dnaG to rpoD) to be 1:2.7:5.1.

10/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09406489 97378267 PMID: 9234948
Minimum protein requirements for transcription and **RNA** replication of a minigenome of human parainfluenza virus type 3 and evaluation of the rule of six.
Durbin AP; Siew JW; Murphy BR; Collins PL
Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892-0720, USA.
Virology (UNITED STATES) Jul 21 **1997**, 234 (1) p74-83, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A reconstituted transcription and **RNA** replication system for human parainfluenza virus type 3 (HPIV3) was developed using components expressed intracellularly from transfected plasmids driven by T7 **RNA polymerase** supplied by a vaccinia virus recombinant. The system is based on a negative-sense **analog** of HPIV3 genomic **RNA** in which the viral genes were deleted and replaced with that encoding bacterial chloramphenicol acetyl transferase (CAT). The N, P, and L proteins expressed from cotransfected plasmids were necessary and sufficient to direct efficient transcription and **RNA** replication. Transcription yielded subgenomic polyadenylated mRNA, which was isolated by oligo(dT)

chromatography. **RNA** replication yielded a mini-antigenome and progeny minigenome, which were shown to be encapsidated based on resistance to digestion with micrococcal nuclease. A panel of cDNAs was constructed to encode minigenomes which differed in length by single-nucleotide increments. Transcription and **RNA** replication in the reconstituted system were most efficient for the minigenome whose length was an even multiple of six. Both **RNA** replication and transcription appeared to be governed by the rule. However, minigenomes whose lengths were one nucleotide greater than or less than an even multiple of six also were very active, especially in **RNA** replication, indicating that the rule was not absolute.

10/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09344246 97329339 PMID: 9185852

The presence of two tightly bound Zn2+ ions is essential for the structural and functional integrity of yeast **RNA polymerase** II.

Mayalagu S; Patturajan M; Chatterji D
Centre for Cellular and Molecular Biology, Hyderabad, (A.P.), India.

Gene (NETHERLANDS) Apr 29 **1997**, 190 (1) p77-85, ISSN 0378-1119 Journal Code: FOP
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

DNA-dependent **RNA polymerases** (RNApol) are Zn2+ metalloproteins where the Zn2+ ion plays both catalytic and structural roles. Although the ubiquitous presence of Zn2+ with the RNApol from eukaryotes had already been established, the exact stoichiometry of Zn2+ ion(s) per mole enzyme is not well documented, and its role in enzymatic function remains elusive. We show here that RNApolII from Saccharomyces cerevisiae has two Zn2+ ions tightly associated with it which are necessary for its transcriptional activity. Upon prolonged dialysis against 10 mM EDTA for 4-5 h, the enzyme loses one Zn2+, as well as partial activity. However, Zn2+ can be added back to the enzyme, but without recovering its total activity. 5 mM orthophenanthroline (OP) removes one Zn2+ within 2 h; the enzyme, however, cannot be reconstituted back with Zn2+. Circular dichroism (CD) studies showed that the conformation of the native enzyme is unique and cannot be reproduced with Zn2+-reconstituted RNApolII. Similarly, the rate of abortive synthesis of a dinucleotide product over a non-specific template is faster when catalyzed by two Zn2+-native enzymes. Zn2+-reconstituted RNApolII or one Zn2+-RNApolII showed a slower abortive synthesis rate. 65Zn2+-blotting experiments indicated that the removal of one Zn2+ from the enzyme destroys the Zn2+-binding ability of the larger subunits of yeast RNApolII. In order to check whether the presence of Zn2+ ions has any effect on substrate recognition, we followed the binding of (gamma-AmNS)UTP, a fluorescent substrate **analog** to RNApolII. It was observed that OP-treated enzyme showed non-specific substrate recognition, whereas two Zn2+-native RNApol binds substrate at a single site.

10/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09201177 97115753 PMID: 8954555

Real-time fluorescence assay system for gene transcription: simultaneous observation of protein/DNA binding, localized DNA melting, and mRNA production.

Dunkak KS; Otto MR; Beechem JM
Department of Molecular Physiology and Biophysics, Vanderbilt University School of Medicine, Nashville, Tennessee, 37232, USA.

Analytical biochemistry (UNITED STATES) Dec 15 **1996**, 243 (2) p234-44, ISSN 0003-2697 Journal Code: 4NK

Contract/Grant No.: GM45990, GM, NIGMS; RR5823, RR, NCRR; T32GM08320, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

This article describes the development of an in vitro multicolor fluorescence assay system for studying protein/DNA complex formation, transcription bubble formation, and mRNA production. These studies were accomplished using three different fluorescent spectroscopic probes: rhodamine-labeled DNA (at the 5' position) to monitor protein/DNA complex formation, DNA internally labeled with the base **analog** 2-aminopurine in place of adenine to monitor transcription bubble formation, and gamma-fluorophore-labeled UTP nucleotide to measure mRNA transcription rates. Combining these three assay systems allows the simultaneous determination of protein/DNA binding, localized DNA melting transitions, and mRNA production at physiological concentrations of reagents (pM-nM) and millisecond timing resolution. The application of this multicolor fluorescence assay to Escherichia coli **RNA polymerase** reactions (binding, open complex formation, and mRNA production) demonstrates the importance of kinetically coupled events in gene transcription.

10/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09200348 96242326 PMID: 9026454

The rpoD gene functions as a multicopy suppressor for mutations in the chaperones, CbpA, DnaJ and DnaK, in Escherichia coli.

Shiozawa T; Ueguchi C; Mizuno T
Laboratory of Molecular Microbiology, School of Agriculture, Nagoya University, Japan.

FEMS microbiology letters (NETHERLANDS) May 1 **1996**, 138 (2-3) p245-50, ISSN 0378-1097 Journal Code: FML
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The CbpA protein is an **analog** of the DnaJ molecular chaperone of Escherichia coli. The dnaJ- cbpA- double-null mutant exhibits severe defects in cell growth, namely, a very narrow temperature range for growth. To gain insight into the functions of CbpA as well as DnaJ, we isolated a multicopy suppressor gene that permits this dnaJ- cbpA- mutant to grow normally at low temperatures. The suppressor gene was identified as rpoD, the gene that encodes the major sigma 70. The biological implications of this finding are examined and discussed.

10/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09198070 97113534 PMID: 8955394

Cloning of the rpoD **analog** from Rhizobium etli: sigA of R. etli is growth phase regulated.

Luka S; Patriarca EJ; Riccio A; Iaccarino M; Defez R
International Institute of Genetics and Biophysics, CNR, Naples, Italy.

Journal of bacteriology (UNITED STATES) Dec **1996**, 178 (24) p7138-43, ISSN 0021-9193 Journal Code: HH3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Rhizobium bacteria fix atmospheric nitrogen during symbiosis with legume plants only after bacterial division is arrested. The role of the major vegetative sigma factor, SigA, utilized by Rhizobium bacteria during symbiosis is unknown. By using PCR technology, a portion of the sigA gene corresponding to domain II was directly amplified from Rhizobium etli total

DNA by using two primers designed in accordance with the published sequence of sigA from Agrobacterium tumefaciens. The amplified fragment was cloned and used as a hybridization probe for cloning of the R. etli sigA gene. Sequencing data revealed an open reading frame of 2,055 bp showing extensive similarity to various vegetative sigma factors. The 5' end of the sigA transcript was determined and revealed a long, seemingly untranslated region of 170 nucleotides. Quantitative analysis of the sigA transcript by RNase protection and by primer extension assays indicated its down-regulation during entry into the stationary phase. On the basis of the structures of various vegetative sigma factors and considering previous information on heterologous expression, we speculate on the function of domain I of vegetative sigma factors.

10/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09196952 97121268 PMID: 8961934
A direct real-time spectroscopic investigation of the mechanism of open complex formation by T7 **RNA polymerase**.
Sastry SS; Ross BM
Laboratory of Molecular Genetics, Rockefeller University, New York, New York 10021, USA. sastrys@rockvax.rockefeller.edu
Biochemistry (UNITED STATES) Dec 10 **1996**, 35 (49) p15715-25, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Initiation of transcription occurs through a series of steps starting with the binding of **RNA polymerase** to a promoter DNA and formation of a closed complex. The closed complexes, then isomerize to open complexes. In the open complexes a portion of the promoter DNA is unwound. Using fluorescence spectroscopy, we have investigated in real-time the mechanism of unwinding of promoter DNA during the transition from closed to open complexes of T7 **RNA polymerase** . We synthesized DNA templates containing the fluorescent base **analog** 2-aminopurine in place of adenine at specific positions in a T7 **RNA polymerase** promoter. We located the 2-aminopurine residues in the presumed melting domain of the promoter at -1, -4, and at -6. The fluorescence of 2-aminopurine increases when the DNA goes from a double-stranded form to a single-stranded form. By spectroscopically monitoring the increase in fluorescence of 2-aminopurine in DNA-T7 **RNA polymerase** complexes, we obtained kinetic and thermodynamic information for DNA unwinding. In the presence of the initiating nucleotide GTP, conformational transitions in the **polymerase** -promoter complex leading to strand opening were slower than in its absence. The rate of base pair disruption at -1, -6, and at -4 was also slower in the presence of GTP than in its absence. At 37 degrees C, base pair disruption occurred first at -1 followed by -6 and finally at -4. Open complex formation was temperature-sensitive. Temperature effects at -1, -6, and at -4 were consistent with this order of base pair disruption. The apparent activation energies (Ea) for base pair disruption around -1 and -6 were 14 kcal mol-1 and 50 kcal mol-1, respectively, also suggesting this order of base pair disruption. Transcription initiation assays using G-ladder synthesis revealed that initiation rates were almost the same on all three templates containing the modified base. Unlike strand opening, we did not observe lag times for G-ladder synthesis. We suggest that facile base pair disruption at -1 is sufficient for transcription initiation. Based on these data, it is proposed that the **polymerase** makes contacts at or near -1 and -6 resulting in untwisting of these base pairs thus creating at least two base pair disruption events at -1 and at -6, which are followed by bidirectional propagation to -4.

10/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09196141 97085415 PMID: 8931555
Thermodynamic and kinetic measurements of promoter binding by T7 **RNA polymerase**.
Ujvari A; Martin CT
Department of Chemistry, University of Massachusetts, Amherst 01003-4510, USA.
Biochemistry (UNITED STATES) Nov 19 **1996**, 35 (46) p14574-82, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Previous steady state kinetic studies of the initiation of transcription by T7 **RNA polymerase** have shown that melting of the DNA helix near the transcription start site is not rate limiting [Maslak, M., & Martin, C. T. (1993) Biochemistry 32, 4281-4285]. In the current work, fluorescence changes in a nucleotide **analog** incorporated within the promoter are used to monitor changes in the DNA helix associated with **polymerase** binding. The fluorescence of 2-aminopurine has been previously shown to depend on the environment of the base, with fluorescence increasing in the transition from a double-stranded to a single-stranded environment [Xu, D., Evans, K.O., & Nordlund, T. M.(1994) Biochemistry 33, 9592-9599]. Fluorescence changes associated with **polymerase** binding to promoters incorporating 2-aminopurine at positions -4 through -1 support a model which includes melting, in the statically bound complex, of the region of the promoter near the start site. Equilibrium titrations at 25 degrees C with label at position -2 provide a thermodynamic measure of the dissociation constant (Kd = 4.8 nM) for promoter binding, while stopped-flow kinetic assays measure the apparent association (k1 = 5.6 x 10(7) M-1 s-1) and dissociation (k-1 = 0.20 s-1) rate constants for simple promoter binding (the ratio k-1/k1 = 3.6 nM, in good agreement with the thermodynamic measurement of Kd). These results suggest that binding is close to the diffusion-controlled limit and helix melting is extremely rapid. In studies of structurally altered promoters, a base functional group substitution at position -10 is shown to significantly decrease k1, with little effect on k-1. In contrast, removal of the nontemplate strand from position +1 downstream results in a large decrease in k-1, with no significant effect on k1.

10/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09142436 97114083 PMID: 8955902
RNAs mediating cotranslational insertion of selenocysteine in eukaryotic selenoproteins.
Hubert N; Walczak R; Sturchler C; Myslinski E; Schuster C; Westhof E; Carbon P; Krol A
UPR 9002 du CNRS, Structure des Macromolecules Biologiques et Mecanismes de Reconnaissance, IBMC, Strasbourg, France.
Biochimie (FRANCE) **1996**, 78 (7) p590-6, ISSN 0300-9084 Journal Code: A14
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Selenocysteine, a selenium-containing **analog** of cysteine, is found in the prokaryotic and eukaryotic kingdoms in active sites of enzymes involved in oxidation-reduction reactions. Its biosynthesis and cotranslational insertion into selenoproteins is performed by an outstanding mechanism, implying the participation of several gene products. The tRNA(Sec) is one of these. In eukaryotes, its transcription mode by **RNA polymerase** III differs from that of classical tRNA genes,

both at the level of the promoter elements and transcription factors involved. In addition, enhanced transcription is afforded by a newly characterized zinc finger activator. Not only transcription of the gene, but also the tRNA(Sec) itself is atypical since its 2D and 3D structures exhibit features which set it apart from classical tRNAs. Decoding of eukaryotic selenocysteine UGA codons requires a stem-loop structure in the 3'UTR of mRNAs, the selenocysteine insertion sequence (SECIS) element. Structure probing and sequence comparisons led us to propose a 2D structure model for the SECIS element, containing a novel **RNA** motif composed of four consecutive non-Watson-Crick base-pairs. A 3D model, rationalizing the accessibility data, was elaborated by computer modeling. It yields indicative or suggestive evidence for the role that could play some conserved residues and/or structural features in SECIS function. These might act as signals for interaction with SBP, the SECIS binding protein that we have characterized.

10/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09095640 97115848 PMID: 8955150
Mapping the contacts of yeast TFIIIB and **RNA polymerase** III at various distances from the major groove of DNA by DNA photoaffinity labeling.
Persinger J; Bartholomew B
Department of Medical Biochemistry, School of Medicine, Southern Illinois University at Carbondale, Carbondale, Illinois 62901-4413, USA.
Journal of biological chemistry (UNITED STATES) Dec 20 **1996**, 271 (51) p33039-46, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM 48413-02, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The structure of the Saccharomyces cerevisiae **RNA polymerase** III transcription complex on the SUP4 tRNATyr gene was probed at distances of approximately 10 to approximately 23 A from the C-5 methyl of thymidine in the major groove of DNA using photoreactive aryl azides attached to deoxyuridine by variable chain lengths. The nucleotide **analogs** contained an azidobenzoyl group attached with chain lengths that were incrementally increased by approximately 4. 3 A by inserting 1-3 glycine residues into the chain. Another photoreactive deoxyuridine **analog** was made that contained a butyl chain (ABU-dUMP) to assess the effect of the chain's hydrophobicity on its ability to photoaffinity label the transcription complex. These nucleotide **analogs** were incorporated at base pairs (bp) -26/-21, -17, or -3/-2 on the nontranscribed strand of the SUP4 tRNATyr gene along with an [alpha-32P]dNMP by primer extension using an immobilized single-stranded DNA template annealed to specific oligonucleotides. The 27-kDa subunit of TFIIIB or the TATA box binding protein was photoaffinity labeled at bp -26/-21 with nucleotide **analogs** containing a approximately 19- or approximately 23-A chain and not with shorter chains of approximately 10 to approximately 15 A in length. The B" subunit of TFIIIB (Mr = 90 kDa) was photoaffinity labeled at bps -26/-21 with DNA containing a approximately 14-A chain and not with shorter or longer chains. Cross-linking of the B" subunit was inhibited by binding of **RNA polymerase** III (Pol III) to the TFIIIB-DNA complex and suggested that Pol III binding causes a conformational change in the TFIIIB-DNA complex resulting in the displacement of the 90-kDa subunit at bps -26/-21. Next, the chain length dependence of photoaffinity labeling the 34-kDa subunit of Pol III at bps -17 and -3/-2 indicated that the 34-kDa subunit of Pol III is slightly removed from the major groove at bp -17 in the initiation complex and makes closer contact at bps -3/-2 in a stalled elongation complex.

10/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09088740 97098436 PMID: 8942976
Cocrystal structure of YY1 bound to the adeno-associated virus P5 initiator.
Houbaviy HB; Usheva A; Shenk T; Burley SK
Laboratory of Molecular Biophysics, Rockefeller University, New York, NY 10021-6399, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Nov 26 **1996**, 93 (24) p13577-82, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Ying-Yang 1 protein (YY1) supports specific, unidirectional initiation of messenger **RNA** production by **RNA polymerase** II from two adjacent start sites in the adeno-associated virus P5 promoter, a process which is independent of the TATA box-binding protein (TBP). The 2.5-A resolution YY1-initiator element cocrystal structure reveals four zinc fingers recognizing a YY1-binding consensus sequence. Upstream of the transcription start sites protein-DNA contacts involve both strands and downstream they are virtually restricted to the template strand, permitting access to the active center of **RNA polymerase** II and ensuring specificity and directionality. The observed pattern of protein-DNA contacts also explains YY1 binding to a preformed transcription bubble, and YY1 binding to a DNA/**RNA** hybrid **analog** of the P5 promoter region containing a nascent **RNA** transcript. A model is proposed for YY1-directed, TBP-independent transcription initiation.

10/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08946346 96312898 PMID: 8703956
Probing the protein-DNA contacts of a yeast **RNA polymerase** III transcription complex in a crude extract: solid phase synthesis of DNA photoaffinity probes containing a novel photoreactive deoxycytidine **analog**.
Lannutti BJ; Persinger J; Bartholomew B
Department of Medical Biochemistry, School of Medicine, Southern Illinois University at Carbondale 62901-4413, USA.
Biochemistry (UNITED STATES) Jul 30 **1996**, 35 (30) p9821-31, ISSN 0006-2960 Journal Code: A0G
Contract/Grant No.: GM 48413-02, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A novel photoreactive deoxycytidine **analog**, 4-[N-(p-azidobenzoyl)-2-aminoethyl]-dCTP (ABdCTP), has been synthesized and incorporated at specific sites within the SUP4 tRNA(Tyr) gene. Immobilized single-stranded DNA was annealed to specific oligonucleotides and AB-dCMP incorporated into DNA by primer extension. DNA photoaffinity labeling with AB-dCMP was used to survey protein-DNA contacts in initiation and elongation complexes of **RNA polymerase** III (Pol III), and compared to DNA photoaffinity labeling using the previously described photoreactive deoxyuridine **analog**, 5-[N-(pazidobenzoyl)-3-aminoallyl] -dUMP (AB-dUMP) [Bartholomew et al. (1993) Mol. Cell.Biol. 13,942-952]. In contrast to previous studies, we have used a crude protein fraction rather than highly purified preparations of Pol III and transcription factors TFIIIC and TFIIIB to examine if some component of the transcription complex is lost upon purification. Eleven nucleotide positions from bp-17 to bp +17 (+1 being the start site of transcription) on the nontranscribed strand were modified and shown to have little or no effect on transcription

complex formation, initiation, or elongation as determined by multiple-round transcription assays. Efficient photoaffinity labeling by DNA containing AB-dCMP gave results comparable to that with AB-dUMP at proximal nucleotide positions and provided new evidence for the placement of the 160 and 31 kDa subunits of Pol III near the 5' end of the transcriptional bubble in an elongation complex. A novel 40 kDa protein was cross-linked at bps -17, -9, and -8 in a TFIIIC-dependent manner that had not been previously detected.

10/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08895582 95271664 PMID: 7752239
A zinc-binding region in the beta' subunit of **RNA polymerase** is involved in antitermination of early transcription of phage HK022.
Clerget M; Jin DJ; Weisberg RA
Section on Microbial Genetics, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20892, USA.
Journal of molecular biology (ENGLAND) May 12 **1995**, 248 (4) p768-80, ISSN 0022-2836 Journal Code: J6V
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Antitermination of early transcription in phage HK022 requires no virus-encoded proteins and thus differs from antitermination by other lambdoid phages. It does require cis-acting phage sequences, which may be **analogous** to the lambdoid nut sites. To identify host proteins involved in antitermination, we isolated 14 Escherichia coli mutants that are specifically blocked in HK022 growth. The mutations are located in the rpoC gene, which encodes the beta' subunit of **RNA polymerase**. Each mutation alters one of three amino acid residues located within a cluster of four completely conserved cysteine residues that are believed to bind zinc. We examined the effect of one mutation on HK022 antitermination in vivo. rpoCY75N greatly reduced readthrough of a strong rho-independent transcription terminator placed downstream of the HK022 PL promoter and nutL **analog**, but did not decrease promoter activity. Purified enzyme had a similar effect on PL-directed transcription in vitro: wild-type but not mutant **polymerase** read through a strong rho-independent terminator located immediately downstream of the nutL **analog** with high efficiency. We suggest that interaction of the putative zinc-binding domain of the **RNA polymerase** beta' subunit with the HK022 antitermination sites suppresses transcription termination, and that this interaction can occur in the absence of other proteins.

10/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08894055 95229650 PMID: 7713937
Regulation of rDNA transcription factors during cardiomyocyte hypertrophy induced by adrenergic agents.
Hannan RD; Luyken J; Rothblum LI
Sigfried and Janet Weis Center for Research, Geisinger Clinic, Danville, Pennsylvania 17822, USA.
Journal of biological chemistry (UNITED STATES) Apr 7 **1995**, 270 (14) p8290-7, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM46991, GM, NIGMS; HL 47638, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Ribosomal DNA transcription is important to the regulation of cardiomyocyte ribosome content and, as a consequence, the rate of protein synthesis and accumulation during cardiac hypertrophy. We studied the

regulation of ribosomal **RNA** synthesis and the levels of **RNA polymerase** I and the ribosomal DNA transcription factor, UBF, during norepinephrine-induced hypertrophy of contraction-arrested neonatal cardiomyocytes in culture. Nuclear run-on assays and Western blots demonstrated that, concomitant with hypertrophy, norepinephrine (1 microM) increased the rate of ribosomal DNA transcription, without causing an increase in the amount of **RNA polymerase** I. However, the elevated rate of rRNA synthesis was accompanied by an increased cellular content of UBF protein as determined by Western analysis. Northern blots demonstrated norepinephrine-induced increases in UBF mRNA in neonatal cardiomyocytes indicating that the response was regulated, at least in part, at the pretranslational stage. Both alpha- and beta-adrenergic agents increased the level of UBF mRNA. The beta-adrenergic response was mimicked by forskolin (1 microM) and the cyclic AMP **analog** dibutyryl cAMP (10 microM). However, activation of protein kinase C by phorbol 12-myristate 13-acetate (0.1 microM) did not increase expression of UBF. These results implicate UBF as a possible regulatory factor of the accelerated rDNA transcription observed during norepinephrine-mediated cardiomyocyte hypertrophy.

10/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08839202 96185023 PMID: 8612682

Inhibition of **RNA polymerase** II transcription causes chromatin decondensation, loss of nucleolar structure, and dispersion of chromosomal domains.

Haaf T; Ward DC
Max-Planck-Institute of Molecular Genetics, Berlin, Germany.
Experimental cell research (UNITED STATES) Apr 10 **1996**, 224 (1) p163-73, ISSN 0014-4827 Journal Code: EPB
Contract/Grant No.: HG-00246, HG, NHGRI; HG-00272, HG, NHGRI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Fluorescence in situ hybridization and immunofluorescence have been used to visualize specific genomic DNA sequences and proteins in interphase nuclei treated with transcriptional inhibitors. The adenosine **analog** 5,6-dichloro-beta-D-ribofuranosylbenzimidazole (DRB) and alpha-amanitin selectively inhibit transcription by **RNA polymerase** II at low doses. Upon exposure to DRB or alpha-amanitin the fibrillar components of the normally compact nucleolus unravel into necklace-like structures which represent highly extended linear arrays of ribosomal (r)**RNA** genes. Similarly, blocks of tandemly repeated satellite DNAs dissociate into extended beaded strands. Localized (euchromatic) chromosome domains and even whole chromosome territories disperse throughout the nuclear interior. Treatment of cells with actinomycin D (AMD) at doses that block rRNA synthesis does not cause significant decondensation of nucleolar, heterochromatic, and interphase chromosome domains. Interestingly, both alpha-amanitin and AMD cause coilin to associate with the nucleolar domain. In AMD-treated cells, coilin is enriched in nucleolar caps abutting upon the residual nucleolus. After alpha-amanitin treatment, coilin is concentrated in numerous beads closely associated with individual rDNA transcription units within nucleolar necklaces. The changes in higher-order nuclear structure are reversible in cell cultures exposed to nontoxic doses of transcriptional inhibitors. It therefore may be concluded that nuclear topographic organization is dependent on a continued transcription of nuclear genes, but not of the rRNA genes.

10/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

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         (c) 2002 BIOSIS

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              39  2(W)THIOCYTIDINE
             140  PYRROLOPYRIMIDINE
           11329  INOSINE
         5051946  2
              75  THIOTHYMIDINE
              11  2(W)THIOTHYMIDINE
         5051946  2
               0  AMINOADENOSIN
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              84  THIOCYTIDINE
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 3/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10365820   99436120   PMID: 10506170
   Bipartite  modular structure of intrinsic, RNA hairpin-independent
termination signal for phage RNA polymerases.
  Kwon YS; Kang C
  Department  of  Biological  Sciences, Korea Advanced Institute of Science
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and Technology, 373-1 Kusong-dong, Yusong-gu, Taejon 305-701, Korea.
Journal of biological chemistry (UNITED STATES) Oct 8 **1999**, 274 (41) p29149-55, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The phage SP6 **RNA** and T7 **RNA polymerases**, which are closely related to each other, intrinsically stop at two signals in the Escherichia coli rrnB terminator t1 through different mechanisms. The downstream signal functioned without an **RNA** secondary structure formation, in which the signal was still active when separated from the upstream, hairpin-forming signal, and IMP incorporation enhanced its efficiency. The sequence from -15 to -1 was essential for the downstream, hairpin-independent termination (at -1). The results of SP6 transcription with heteroduplex templates and ribonucleotide **analogs** suggested that the downstream signal consists of two functionally different modules. The effects of iodo-CMP or IMP incorporation into **RNA** on termination efficiency were not sensitive to incorporation at -9 and upstream, but they were reactive to incorporation at -6 and -2, as reflected by strong iodo-rC:dG and weak rI:dC base pairing. Thus, the downstream module (from -8 approximately -6 to -1) appears to facilitate the release of **RNA**. Mismatches in the templates at -6 to +1 allowed for efficient termination, unlike those upstream of the sequence. The upstream module (from -15 to -9 approximately -7) functions as a duplex. Pausing of the SP6 elongation complex at the termination site was detected when **RNA** release was suppressed by the incorporation of 5-bromo-UMP, and it was dependent on the upstream module. Results of single-round SP6 transcriptions using 3'-deoxynucleotides and immobilized templates indicated that **RNA** was not released from the elongation complexes halted at the termination site on the template variants carrying mutations in the upstream or downstream module, whereas such complexes on the wild type template were dissociated. Thus, halting or simple pausing was not sufficient for termination even when the downstream module was intact. The upstream module appears to mediate such conformation change necessary for termination.

3/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09988073 99032996 PMID: 9813225

Identification of stable **RNA** hairpins causing band compression in transcriptional sequencing and their elimination by use of **inosine** triphosphate.

Sasaki N; Izawa M; Sugahara Y; Tanaka T; Watahiki M; Ozawa K; Ohara E; Funaki H; Yoneda Y; Matsuura S; Muramatsu M; Okazaki Y; Hayashizaki Y
Laboratory for Genome Exploration Research Project, Genomic Sciences Center (GSC) and Genome Science Laboratory, Tsukuba Life Science Center, The Institute of Physical and Chemical Research (RIKEN), 3-1-1 Koyadai, Tsukuba, Ibaraki 305-0074, Japa.

Gene (NETHERLANDS) Nov 5 **1998**, 222 (1) p17-23, ISSN 0378-1119 Journal Code: FOP
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

To identify stable **RNA** secondary structure causing band compression, 30 lambda DNA clones and four cDNA clones (about 10 kb in total length) were sequenced using Transcriptional Sequencing, which is based on the phage **RNA polymerase** chain termination reaction with fluorescent 3' deoxynucleoside triphosphate, using the canonical set of rNTPs for the substrate. Electrophoresis was performed on acrylamide gel containing 7 M urea at 50 degrees C using ABI 377 DNA sequencer. A total of 159 band compressions were identified, and most compression sites seem to be due to hairpin structures. We also found that the presence of rITP in place of rGTP in the sequencing reaction can entirely eliminate all band

compressions. The use of rITP gave a better peak uniformity and resolution in the sequencing gel in the case of lambda DNA than with c7rGTP, leading to improved accuracy in the sequence determination. Substitution of the base **analog** rITP for rGTP should be useful for accurate sequencing determination.

3/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09924931 98416185 PMID: 9742229
The use of diaminopurine to investigate structural properties of nucleic acids and molecular recognition between ligands and DNA.
Bailly C; Waring MJ
INSERM U-124 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Place de Verdun, 59045 Lille, France. bailly@lille.inserm.f
Nucleic acids research (ENGLAND) Oct 1 **1998**, 26 (19) p4309-14, ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
2,6-Diaminopurine (DAP) is an **analogue** of adenine which can be converted to nucleotides that serve as substrates for incorporation into nucleic acids by **polymerases** in place of (d)AMP. It pairs with thymidine (or uracil), engaging in three hydrogen bonds of the Watson-Crick type. The result of DAP incorporation is to add considerable stability to the double helix and to impart other structural features, such as an altered groove width and disruption of the normal spine of hydration. DNA containing DAP may or may not be recognized by restriction endonucleases; **RNA** containing DAP may not engage in normal splicing. The DAP.T pair affects the local flexibility of DNA and impedes the interaction with helix bending proteins. By providing a non-canonical hydrogen bond donor in the minor groove and/or blocking access to the floor of that groove it strongly affects interactions with small molecules such as antibiotics and anticancer drugs. Examples which illustrate altered recognition of nucleotide sequences in DAP-containing DNA are presented: changed sites of cutting by bleomycin, photocleavage by uranyl nitrate and footprinting with mithramycin. Using DNA in which both A-->DAP and G-->**Inosine** substitutions have been made it is possible to assess precisely the role of the purine 2-amino group in ligand-DNA recognition.

3/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09888455 98409449 PMID: 9737873
Identifying **RNA** minor groove tertiary contacts by nucleotide **analogue** interference mapping with N2-methylguanosine.
Ortoleva-Donnelly L; Kronman M; Strobel SA
Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, Connecticut 06520, USA.
Biochemistry (UNITED STATES) Sep 15 **1998**, 37 (37) p12933-42, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Nucleotide **analogue** interference mapping (NAIM) is a general biochemical method that rapidly identifies the chemical groups important for **RNA** function. In principle, NAIM can be extended to any nucleotide that can be incorporated into an in vitro transcript by an **RNA polymerase**. Here we report the synthesis of 5'-O-(1-thio)-N2-methylguanosine triphosphate (m2GalphaS) and its incorporation into two reverse splicing forms of the Tetrahymena group I intron using a mutant form of T7 **RNA polymerase**. This

analogue replaces one proton of the N2 exocyclic amine with a methyl group, but is as stable as guanosine (G) for secondary structure formation. We have identified three sites of m2GalphaS interference within the Tetrahymena intron: G22, G212, and G303. All three of these guanosine residues are known to utilize their exocyclic amino groups to participate in tertiary hydrogen bonds within the ribozyme structure. Unlike the interference pattern with the phosphorothioate of **inosine** (IalphaS, an **analogue** that deletes the N2 amine of G), m2GalphaS substitution did not cause interference at positions attributable to secondary structural stability effects. Given that the **RNA** minor groove is likely to be widely used for helix packing, m2GalphaS provides an especially valuable reagent to identify **RNA** minor groove tertiary contacts in less well-characterized RNAs.

3/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09691715 98169155 PMID: 9510335
Enzymatic incorporation of 2'-thio-CTP into the HDV ribozyme.
Raines K; Gottlieb PA
Department of Biological Science, SUNY at Buffalo, New York 14260, USA.
RNA (UNITED STATES) Mar **1998**, 4 (3) p340-5, ISSN 1355-8382
Journal Code: CHB
Contract/Grant No.: GM52033, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have synthesized the **analogue** 2'-deoxy-2'-thio-CTP (CTP-SH) and tested its ability to support **RNA** transcription in place of CTP. The modified nucleotide in a transcription reaction and in the absence of CTP generated the appropriately sized fragment when a mutant T7 **polymerase** (Y639F) was used. Wild-type **polymerase** was unable to generate **RNA** under the same conditions. Transcription was optimal around pH 7.5 and was dependent upon CTP-SH concentration. Transcripts containing the **analogue** were efficiently isolated using a thiol-activated sepharose column. Insertion of CTP-SH into the HDV ribozyme, replacing all cytidine residues with **2'-thiocytidine**, appears to inhibit self-cleaving activity, even in the presence of manganese. The ability to introduce the CTP-SH **analogue** enzymatically into **RNA** opens the way for new structure-function studies where the 2'-hydroxyl can be efficiently replaced by a thiol group.

3/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09524279 97095015 PMID: 8940436
Group-specific identification of polioviruses by PCR using primers containing mixed-base or deoxyinosine residue at positions of codon degeneracy.
Kilpatrick DR; Nottay B; Yang CF; Yang SJ; Mulders MN; Holloway BP; Pallansch MA; Kew OM
Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Center for Disease Control and Prevention, Atlanta, Georgia 30333, USA. dyk0@ciddvdl.em.cdc.gov
Journal of clinical microbiology (UNITED STATES) Dec **1996**, 34 (12) p2990-6, ISSN 0095-1137 Journal Code: HSH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have developed a method for differentiating polioviruses from nonpolio enteroviruses using PCR. A pair of panpoliovirus PCR primers were designed to match intervals encoding amino acid sequences within VP1 that are

strongly conserved among polioviruses. The initiating primer hybridizes with codons of a 7-amino-acid sequence that has been found only in polioviruses; the second primer matches codons of a domain thought to interact with the cell receptor. The panpoliovirus PCR primers contain mixed-base and deoxyinosine residues to compensate for the high degeneracy of the targeted codons. All RNAs from 48 vaccine-related and 110 wild poliovirus isolates of all three serotypes served as efficient templates for amplification of 79-bp product. None of the genomic sequences of 49 nonpolio enterovirus reference strains were amplified under equivalent reaction conditions. Sensitivities of poliovirus detection were as low as 100 fg (equivalent to approximately 25,000 genomic copies or 25 to 250 PFU) when the amplified products were visualized by ethidium bromide fluorescence. These degenerate PCR primers should aid in the detection of all polioviruses, including those wild poliovirus isolates for which genotype-specific reagents are unavailable.

3/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09202194 97169228 PMID: 9016675
Selective amplification of **RNA** utilizing the nucleotide **analog** dITP and Thermus thermophilus DNA **polymerase**.
Auer T; Sninsky JJ; Gelfand DH; Myers TW
Program in Core Research, Roche Molecular Systems, Alameda, CA 94501, USA.
Nucleic acids research (ENGLAND) Dec 15 **1996**, 24 (24) p5021-5, ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The ability to selectively amplify **RNA** in the presence of genomic DNA of **analogous** sequence is cumbersome and requires implementation of critical controls for genes lacking introns. The convenient approaches of either designing oligonucleotide primers at the splice junction or differentiating the target sequence based on the size difference obtained by the presence of the intron are not possible. Our strategy for the selective amplification of **RNA** targets is based on the enzymology of a single thermostable DNA **polymerase** and the ability to modulate the strand separation temperature requirements for PCR amplification. Following reverse transcription of the **RNA** by recombinant Thermus thermophilus DNA **polymerase** (rTth pol), the resulting RNAxDNA hybrid is digested by the RNase H activity of rTth pol, allowing the PCR primer to hybridize and initiate second-strand cDNA synthesis. Substitution of one or more conventional nucleotides with nucleotide **analogs** that decrease base stacking interactions and/or hydrogen bonding (e.g. hydroxymethyldUTP or dITP) during the first- and second-strand cDNA synthesis step reduces the strand separation temperature of the resultant DNAxDNA duplex. Alteration of the thermal cycling parameters of the subsequent PCR amplification, such that the strand separation temperature is below that required for denaturation of genomic duplex DNA composed of standard nucleotides, prevents the genomic DNA from being denatured and therefore amplified.

3/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08778117 96000049 PMID: 8574193
PCR with deoxyinosine-containing primers using DNA **polymerases** with proofreading activity.
Fujiwara H; Fujiwara K; Hashimoto K
Department of Dermatology, Wayne State University, Detroit, Michigan 48201, USA.
PCR methods and applications (UNITED STATES) Feb **1995**, 4 (4)

p239-40, ISSN 1054-9803 Journal Code: BNV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

3/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08733244 96264015 PMID: 8669894
Inhibition of neurotropic mouse retrovirus replication in glial cells by synthetic oligo(2'-O-methyl)ribonucleoside phosphorothioates.
Takase-Yoden S; Shibahara S; Morisawa H; Watanabe R
Institute of Life Science, Soka University, Hachioji, Tokyo, Japan.
Antiviral research (NETHERLANDS) Dec **1995**, 28 (4) p359-68, ISSN 0166-3542 Journal Code: 6I7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Synthetic oligo(2'-O-methyl)ribonucleoside phosphorothioate, FS-25, which is complementary to the splicing acceptor site of neurotropic mouse retrovirus (FrC6 virus), and non-complementary **analogs** including 2'-O-methylinosine homo oligomer (MIS-25), both inhibited viral infection in glial cells. In addition, FS-25 and MIS-25 partially suppressed viral production of glial cells persistently infected with FrC6 virus. Both FS-25 and MIS-25 potently inhibited reverse transcriptase activity of the FrC6 virus in a cell-free system. Addition of these compounds before or after second-round infection of the FrC6 virus inhibited the accumulation of unintegrated viral DNA. These results indicate that these compounds fundamentally inhibit retrovirus production in glial cells in the same manner in which they inhibit HIV production, by blocking several viral replication pathways including fresh infection, second-round infection, and reverse transcription of the viral genome. Our novel neurotropic retrovirus is a useful experimental model for the development of drugs against HIV infection.

3/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08651480 96028205 PMID: 7473705
Effects of base substitutions on the binding of a DNA-bending protein.
Bailly C; Waring MJ; Travers AA
Department of Pharmacology, University of Cambridge, UK.
Journal of molecular biology (ENGLAND) Oct 13 **1995**, 253 (1) p1-7, ISSN 0022-2836 Journal Code: J6V
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In order to investigate whether the 2-amino group of guanine, which lies in the minor groove of the B-form helix, can directly influence DNA flexibility and major groove recognition by proteins we have examined the properties of DNA molecules containing **inosine** and/or 2,6-diaminopurine (DAP) residues. Appropriately substituted tyrT(A93) DNA fragments were prepared by the **polymerase** chain reaction. Their mobility in non-denaturing gels was affected, consistent with changed anisotropic flexibility leading to increased curvature due to G-->I substitution and decreased curvature due to replacement of adenine with DAP. Band-shift assays of FIS protein binding revealed facilitated interaction with **inosine**-containing DNA and markedly reduced binding to DAP-containing DNA, attributable to altered bendability. DNase footprinting experiments confirmed that fewer sites would bind FIS in DAP-containing DNA at a given protein concentration, whereas higher levels of binding occurred with **inosine** -containing molecules. Thus base

substitutions which affect the placement and presence of the purine 2-amino group in the minor groove can affect both the intrinsic curvature and the bendability of DNA.

3/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05915251 88198165 PMID: 2834368
Factor-dependent transcription termination by vaccinia virus **RNA polymerase** . Evidence that the cis-acting termination signal is in nascent **RNA**.
Shuman S; Moss B
Laboratory of Viral Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892.
Journal of biological chemistry (UNITED STATES) May 5 **1988**, 263 (13) p6220-5, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Transcription termination in vitro by vaccinia **RNA polymerase** is dependent on a trans-acting factor, VTF, that is associated with, if not identical to, the vaccinia mRNA capping enzyme. VTF-induced termination occurs approximately 50 nucleotides downstream of a signal sequence TTTTTNT in the non-transcribed templated strand; thus the cognate sequence UUUUUNU is expressed in the nascent **RNA**. To address the role of the nascent **RNA** in chain termination, the effects of nucleotide base **analog** substitutions were studied. Incorporation of bromo- (Br) UMP or iodo- (I) UMP into **RNA** abrogated factor-dependent termination without preventing the synthesis of read-through transcripts. Substitution of either ITP or 7'-methylguanosine for GTP did not inhibit factor-dependent termination, nor did the substitution of BrCTP or ICTP for CTP. The early transcripts synthesized in vitro were sensitive to RNase T2 but resistant to RNase H, indicating an absence of extensive hybridization of **RNA** product to the DNA template. Substitution of BrUTP for UTP did not alter the nuclease sensitivity of the transcripts, suggesting that increased stability of **RNA**:DNA hybrid structures did not account for the **analog** effects. These results are consistent with a model in which recognition of the primary sequence UUUUUNU in nascent **RNA** by the **polymerase** and/or VTF is required for transcription termination.

3/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05889050 86091141 PMID: 2417079
In-vitro inhibition of LAV/HTLV-III infected lymphocytes by dithiocarb and **inosine** pranobex.
Pompidou A; Zagury D; Gallo RC; Sun D; Thornton A; Sarin PS
Lancet (ENGLAND) Dec 21-28 **1985**, 2 (8469-70) p1423, ISSN 0140-6736 Journal Code: L0S
Languages: ENGLISH
Document type: Letter
Record type: Completed

3/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05865907 85236949 PMID: 2861271
Antitumor agents 68: effects of a series of helenalin derivatives on P-388 lymphocytic leukemia nucleic acid and protein synthesis.
Hall IH; Williams WL; Chaney SG; Gilbert CJ; Holbrook DJ; Muraoka O; Kiyokawa H; Lee KH

Journal of pharmaceutical sciences (UNITED STATES) Mar **1985**, 74 (3) p250-4, ISSN 0022-3549 Journal Code: JO7
Contract/Grant No.: CA-17625, CA, NCI; CA-26466, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A series of **analogues** related to helenalin demonstrated moderate capability for inhibiting the growth of murine P-388 lymphocytic leukemia cells in vivo and in vitro. The growth inhibition correlated with suppression of both DNA and protein synthesis in P-388 cells. The inhibition of protein synthesis occurred at a relatively low concentration and appeared to occur at the level of initiation. The suppression of DNA synthesis in P-388 cells correlated positively with inhibition of **inosine** 5'-monophosphate dehydrogenase activity. Although nuclear and alpha DNA **polymerase** activities were suppressed by certain **analogues**, the inhibition of the **polymerases** did not correlate positively with DNA synthesis inhibition and, furthermore, the magnitude of suppression of DNA **polymerase** activity did not appear to be sufficient to account for the observed suppression of DNA synthesis in P-388 cells.

3/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05570364 89227094 PMID: 2469387
Combinations of isoprinosine and 3'-azido-3'-deoxythymidine in lymphocytes infected with human immunodeficiency virus type 1.
Schinazi RF; Cannon DL; Arnold BH; Martino-Saltzman D
Veterans Administration Medical Center, Decatur, Georgia 30033.
Antimicrobial agents and chemotherapy (UNITED STATES) Dec **1988**, 32 (12) p1784-7, ISSN 0066-4804 Journal Code: 6HK
Contract/Grant No.: AI 25899, AI, NIAID; AI 26055, AI, NIAID; SO7 RR05364, RR, NCRR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Since clinical trials are being planned with the immunomodulating drug isoprinosine combined with the antiviral drug 3'-azido-3'-deoxythymidine (AZT) in patients with acquired immunodeficiency syndrome (AIDS) and AIDS-related complex, it is important to determine the type of antiviral interaction produced by these drugs in vitro. Such a combined modality may not only produce enhanced antiviral effects but also may have a valuable immunorestorative action. The interaction of several ratios of AZT and isoprinosine on the replication of human immunodeficiency virus type 1 in human peripheral blood mononuclear cells was determined by reverse transcriptase assay of disrupted virus obtained from supernatants of cells that were exposed to virus and the drugs separately and in combination and by a human immunodeficiency virus type 1 p24 enzyme immunoassay of the same supernatants. The correlation between the reverse transcriptase and enzyme immunoassay data was high. The antiviral activity of AZT alone was neither diminished nor augmented when AZT was used in combination with isoprinosine. Isoprinosine did not enhance virus yield when used alone or in combination with AZT in peripheral blood mononuclear cells, nor did it affect the growth of uninfected cells. The in vitro results indicate that this combination did not decrease the efficacy of AZT or exacerbate virus replication.

3/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05560468 89014351 PMID: 2459590
Factors determining the activity of 2',3'-dideoxynucleosides in

suppressing human immunodeficiency virus in vitro.
Hao Z; Cooney DA; Hartman NR; Perno CF; Fridland A; DeVico AL; Sarngadharan MG; Broder S; Johns DG
Developmental Therapeutics Program, National Cancer Institute, Bethesda, Maryland 20892.
Molecular pharmacology (UNITED STATES) Oct **1988**, 34 (4) p431-5 , ISSN 0026-895X Journal Code: NGR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Mitsuya and Broder [Proc. Natl. Acad. Sci. USA 83:1911-1915 (1986)] demonstrated that every purine (adenosine, guanosine, and **inosine**) and pyrimidine (cytidine and thymidine) nucleoside containing the 2',3'-dideoxyribose configuration, when evaluated against human immunodeficiency virus (HIV) in vitro, significantly suppressed both the infectivity and the cytopathic effect of the virus, with 2',3'-dideoxycytidine (ddCyd) being the most potent of the series (total antiviral protection at 0.5-1.0 microM). We have compared three factors likely to be of significance in determining the pharmacological activity of these compounds, i.e., (i) their abilities to influence pool sizes of physiological deoxynucleoside-5'-triphosphates, (ii) their capacity to generate the corresponding 2',3'-dideoxynucleoside-5'-triphosphates, and (iii) the effectiveness of these nucleoside-5'-triphosphates as inhibitors of HIV reverse transcriptase. In MOLT-4 cells (a human T cell line), ddCyd was the compound most efficiently converted to its 5'-triphosphate, whereas 2',3'-dideoxyguanosine and 2',3'-dideoxythymidine were the compounds least efficiently converted, generating levels of their corresponding 5'-triphosphates less than 0.1% of that seen with ddCyd when these nucleosides were compared on an equimolar basis (5 microM). The 3'-azido **analogue** of 2',3'-dideoxythymidine fell intermediate between these two extremes. As inhibitors of HIV reverse transcriptase, however, all the 5'-triphosphates, with the exception of 2',3'-dideoxyinosine-5'-triphosphate, fell within a narrow range of activity (Ki, 0.10-0.26 microM), affinities some 40-60 fold greater than those of the corresponding physiological 2'-deoxynucleoside-5'-triphosphates. Significant alterations in pool sizes of physiological 2'-deoxynucleoside-5'-triphosphates were not observed at pharmacologically effective drug levels. The relative ability of 2',3'-dideoxynucleosides to generate 5'-triphosphates intracellularly thus correlates much more closely than do the other two factors examined, in capacity to block HIV replication. These studies support the conclusion that, for purposes of design of new compounds of this general class, factors influencing efficiency of nucleotide formation and degradation (e.g., membrane transport mechanisms, affinities for nucleoside kinases and for nucleotide kinases and phosphatases) may be of equal or even greater importance than differences in the relative abilities of the resultant 2',3'-dideoxynucleoside-5'-triphosphates to inhibit the viral reverse transcriptase.

3/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05454212 90137079 PMID: 2515459
Differential effect of collaterally sensitive antimetabolites on P388 murine leukemia sensitive and resistant to adriamycin in vitro.
Satyamoorthy K; Deshpande SS; Chitnis MP
Division of Biology, Kansas State University, Manhattan.
Neoplasma (CZECHOSLOVAKIA) **1989**, 36 (6) p673-83, ISSN 0028-2685 Journal Code: NVO
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Experiments were carried out in vitro using DNA **polymerase** and ribonucleotide reductase inhibitors to investigate their cytotoxicity to

P388 murine leukemia sensitive (P388/S) and resistant (P388/R) to adriamycin (ADR). DNA **polymerase** inhibitors such as cytosine arabinoside (ara-C) and aphidicolin elicited comparative inhibition of DNA biosynthesis in both parental and ADR-resistant tumor cells. However, ribonucleotide reductase inhibitors such as hydroxyurea (HU) and caracemide were collaterally more sensitive to P388/R cells. **Inosine** diglycolaldehyde (Inox) was ineffective in showing such a response. Pretreatment with HU significantly increased intracellular ADR levels and inhibition of **RNA** biosynthesis by ADR in P388/R cells while, in P388/S cells, sequential or concurrent treatment with HU did not enhance intracellular ADR levels. Mechanisms underlying such an effect, implications due to reduced intracellular ATP levels in drug-resistant cells, and the possible utility of using ribonucleotide reductase as a target in drug-resistant tumors for the therapeutic benefit are discussed.

3/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04838957 81053839 PMID: 7001370
Azidopolynucleotides as photoaffinity reagents.
Cartwright IL; Hutchinson DW
Nucleic acids research (ENGLAND) Apr 11 **1980**, 8 (7) p1675-91, ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Polynucleotides containing adenosine and 8-azidoadenosine or **inosine** and 8-azidoinosine residues have been prepared from mixtures of nucleoside diphosphates using polynucleotide phosphorylase from Escherichia coli. These copolymers can form complexes with polyuridylic or polycytidylic acids respectively. Single stranded poly(adenylic, 8-azidoadenylic acid) [poly(A,z8A)] has been used as a photoaffinity reagent to explore the subunit topography of **RNA polymerase** from E. coli.

3/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03478931 79209290 PMID: 454484
Dialdehyde derivative of 5'-deoxyinosine as a more potent **analog** of the dialdehyde derivative of **inosine** (NSC 118994).
Cory JG; Parker SH
Biochemical pharmacology (ENGLAND) Mar 15 **1979**, 28 (6) p867-71, ISSN 0006-2952 Journal Code: 9Z4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

3/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03478901 79209035 PMID: 110317
Form II DNA-dependent **RNA polymerase** from Drosophila melanogaster: general in vitro catalytic properties and template interactions.
Phillips JP
Biochemical genetics (UNITED STATES) Feb **1979**, 17 (1-2) p77-95, ISSN 0006-2928 Journal Code: 9YK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Several in vitro properties of partially purified form II **RNA polymerase** from Drosophila melanogaster embryo nuclei are described. The enzyme preparation is free from contaminating RNase, protein kinase, and polyphosphate kinase activities and can be used to study the incorporation of gamma-32P-labeled nucleoside triphosphates. The enzyme exhibits a biphasic heat inactivation pattern which is probably related to differential lability of its two subforms. However, a considerable protection against heat inactivation is provided by the nucleoside triphosphates present in the in vitro reaction system such that the enzyme catalyzes **RNA** synthesis in a nearly linear mode for over 2 hr at 30 C. Two initiation inhibitors, rifamycin AF/013 was found unsuitable for critical studies because of the high concentrations necessary for total inhibition (200 micrograms/ml) and particularly because of the obligate use of solvents which secondarily have a destabilizing effect on native DNA. Poly[I] was found to effectively block initiation at very low concentrations (1 microgram/ml). The enzyme rapidly forms poly[I]-resistant preinitiation complexes on both double- and single-stranded DNA. These complexes decay with a half-life of 2.5--3 min. **RNA** synthesis from poly[I]-resistant complexes amounts to 10% of the total potential synthesis on both double- and single-stranded DNA. Enzyme-DNA saturation experiments indicate that the form II enzyme discriminates two types of sites on Drosophila DNA, tight binding and weak binding, from which **RNA** synthesis proceeds slowly and rapidly, respectively. The tight-binding sites appear to be **analogous** to those sites with which the enzyme is able to form poly[I]-resistant complexes.

3/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03413073 78248337 PMID: 79996
Inhibition of oncornavirus functions by poly (2-methylthioinosinic acid).
De Clercq E; Billiau A; Hattori M; Ikehara M
Nucleic acids research (ENGLAND) Dec **1975**, 2 (12) p2305-13,
ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Poly (2-methylthioinosinic acid) [poly(ms2I)] was found to markedly inhibit the **RNA** directed DNA **polymerase** (reverse transcriptase) activity of murine (Moloney, Rauscher) leukemia virus and murine (Moloney) sarcoma virus, while under the same conditions the unsubstituted parent compound poly(I) showed little, if any, inhibitory effect. Copolymers of inosinic acid (I) and 2-methylthioinosinic acid2(ms2I) showed an intermediary effect, depending on the I:ms2I ratio. Poly(ms2I) also inhibited the transformation of normal cells by murine (Moloney) sarcoma virus, as assessed by an infectious center assay.

3/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03411095 76268958 PMID: 60741
Role of purine N-3 in the biologic activities of poly(A) and poly(I).
de Clercq E; Torrence PF; Fukui T; Ikehara M
Nucleic acids research (ENGLAND) Jun **1976**, 3 (6) p1591-601,
ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Poly(c3A) (poly 3-deazaadenylic acid) and poly(c3I) (poly 3-deazainosinic acid) differ in biological reactivity from their parent compounds poly(A) and poly(I) and from their 7-deaza counterparts poly(c7A) and poly(c7I). Three parameters of biological reactivity were evaluated : (1 degree)

interferon induction, (2 degrees) anti-complement activity, (3 degrees) reverse transcriptase inhibition. Unlike poly(A)-poly(U), poly(I)-poly(C) and poly(I)-poly(br5C), the mixtures of poly(c3A) + POLY(U), poly(c3I) + poly(C), and poly(c3I) + poly(br5C) failed to elicit an interferon response in "super-induced" primary rabbit kidney cells; Poly(I) and its **analogs** poly(c3I) and poly(c7I) inhibited hemolytic complement activity, whereas poly(A) and its **analogs** poly(c3A) and poly(c7A) failed to do so. Both poly(I) and poly(c7I), but not poly(c3I), lost their anti-complement potency when annealed to either poly(C) or poly(A)-poly(U). Similarly, poly(I) and poly(c7I), but not poly(c3I), suppressed the interferon inducing ability of poly(A)-poly(U), suggesting that both poly(I) and poly(c7I), but not poly(c3I), added to poly(A)-poly(U) to form a triple-helical structure. Poly(I), poly(C7I) and poly(c7A)exerted a distinct inhibitory effect on turine leukemia virus, while under the same conditions poly(c3I) and poly(c3A) showed little, if any, inhibitory effect.

3/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02767324 78130121 PMID: 344317
Termination of transcription by Escherichia coli **RNA polymerase** in vitro is affected by ribonucleoside triphosphate base **analogs**.
Neff NF; Chamberlin MJ
Journal of biological chemistry (UNITED STATES) Apr 10 **1978**, 253 (7) p2455-60, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

3/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02766946 78105212 PMID: 564236
Inhibition of **RNA** synthesis in Ehrlich tumor cells by the dialdehyde derivative of **inosine** (NSC 118994).
Cory JG; Parker SH; Fox CS
Cancer research (UNITED STATES) Mar **1978**, 38 (3) p815-22, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

3/3,AB/24 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09531771 BIOSIS NO.: 199497540141
One-lane chemical sequencing of PCR amplified DNA: The use of terminal transferase and of the base **analogue inosine**.
AUTHOR: Di Mauro Ernesto(a); Costanzo Giovanna; Negri Rodolfo
AUTHOR ADDRESS: (a)Dip. Genetica Biologia Molecule, Univ. Di Roma 'La Sapienza', Piazzle Aldo Movos, 0018T Rome**Italy
JOURNAL: Nucleic Acids Research 22 (18):p3811-3812 **1994**
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English
1994

3/3,AB/25 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08888186 BIOSIS NO.: 199396039687
Binding of guanosine and 3' splice site **analogues** to a group I ribozyme: Interactions with functional groups of guanosine and with additional nucleotides.
AUTHOR: Moran Sean; Kierzek Ryszard; Turner Douglas H(a)
AUTHOR ADDRESS: (a)Dep. Chem., Univ. Rochester, Rochester, NY 14627-0216** USA
JOURNAL: Biochemistry 32 (19):p5247-5256 **1993**
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Dissociation constants, K-d, were measured by equilibrium dialysis at 5 degree C for a series of substrates binding to the L-21 ScaI ribozyme derived from the Tetrahymena thermophila self-splicing large subunit (LSU) ribosomal **RNA** intron. These substrates are **analogues** for the 3' exon splice site, the cyclization site, and the exogenous G that initiates group I splicing. UCG has a K-d of 17 mu-M. Lengthening the substrate to GUCG and GGUCG enhances binding but by less than expected from potential base pairing. Functional groups on the 3'-terminal G of GUCG were replaced with H to test their effect on binding. GUC(2'dG) binds slightly tighter than the all-ribose molecule but shows no reactivity as a substrate. GUC(3'dG) binds weaker than GUCG. **Inosine** and 2-aminopurine ribonucleoside at the 3' position weaken binding by 16- and 26-fold, respectively, but both tetramers are reactive. Thus hydrogen bonds to Watson-Crick pairing positions of the 3'G of GUCG contribute 1-2 kcal/mol to the free energy change for binding. Similar results are found in comparisons of UCG with UC(2'dG), UC(3'dG), and UCI. The nonreactive substrate GUCdGA includes a phosphodiester bond 3' to the guanosine that is the site of chemistry for the all-ribose substrate GUCGA; GUCdGA binds 50 times more weakly than GUCdG. A similar result is obtained for GUCdGU. Competition experiments show that guanosine and guanosine 5'-monophosphate bind with dissociation constants of about 0.9 mM. The monomers 2'dG and 3'dG have K-d's of 0.5 and gtoreq 3 mM, respectively. This suggests that sugar pucker and/or interactions with hydroxyl groups affect binding. Implications for ribozyme catalysis, splicing, cyclization, and design of antisense oligomers are discussed.

1993

3/3,AB/26 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02738529 BIOSIS NO.: 000068049129
DI ALDEHYDE DERIVATIVE OF 5 DEOXY **INOSINE** AS A MORE POTENT **ANALOG** OF THE DI ALDEHYDE DERIVATIVE OF **INOSINE** NSC-118994
AUTHOR: CORY J G; PARKER S H
AUTHOR ADDRESS: DEP. BIOCHEM., COLL. MED., UNIV. S. FLA., TAMPA, FLA. 33612, USA.
JOURNAL: BIOCHEM PHARMACOL 28 (6). 1979. 867-872. **1979**
FULL JOURNAL NAME: Biochemical Pharmacology
CODEN: BCPCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The dialdehyde derivative of 5'-deoxyinosine (5'-deoxyinox) was prepared from 5'-deoxyadenosine by HNO2 deamination and periodate oxidation. 5'-Deoxyinox inhibited ribonucleotide reductase activity in cell-free extracts and inhibited **RNA** and DNA syntheses in intact cells [mouse Ehrlich ascites carcinoma]. Further, 5'-deoxyinox inhibited the conversion of cytidine nucleotides to deoxycytidine nucleotides in intact cells. In comparative studies with the dialdehyde derivative of **inosine** (Inox), 5'-deoxyinox was more active on a molar basis in inhibiting **RNA** or DNA synthesis in intact cells. In addition, 5'-deoxyinox was more inhibitory to the growth of rat Novikoff hepatoma cells in culture than was Inox. 5'-Deoxyinox, in addition to being more active than Inox, also differed from Inox in its biochemical properties. Inox did not inhibit **RNA polymerase** activity when added to isolated nuclei. On the other hand, 5'-deoxyinox showed a marked inhibition of the **RNA polymerase** activity when added to the isolated nuclei. Further, inhibition of the **RNA polymerase** activity in the nuclei from Inox-treated cells was reversed completely by the addition of exogenous polydeoxyadenylate-deoxythymidylate as template, whereas the inhibition caused by 5'-deoxyinox was not reversed by this treatment. In addition to the variation in activity caused by altering the purine component, the nature of the dialdehyde moiety also plays a role in the mode of action of this class of compounds.

1979

3/3,AB/27 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02730394 BIOSIS NO.: 000068040993
TERMINATION OF TRANSCRIPTION BY ESCHERICHIA-COLI **RNA POLYMERASE** INFLUENCE OF SECONDARY STRUCTURE OF **RNA** TRANSCRIPTS ON RHO INDEPENDENT AND RHO DEPENDENT TERMINATION
AUTHOR: ADHYA S; SARKAR P; VALENZUELA D; MAITRA U
AUTHOR ADDRESS: DEP. DEV. BIOL., 1300 MORRIS PARK AVE., BRONX, N.Y. 10461, USA.
JOURNAL: PROC NATL ACAD SCI U S A 76 (4). 1979. 613-1617. **1979**
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of **RNA** secondary structure on .rho.-independent and .rho.-dependent termination of transcription of [phage] T3 DNA by E. coli **RNA polymerase** studied by incorporating, into nascent transcripts, base **analogs** that lead to altered base-pairing properties. A guanine .fwdarw. hypoxanthine substitution, with attendant weakening of secondary structure, abolished the .rho.-independent termination at 20% of the genome; in contrast, replacement of cytosine with 5-bromocytosine, which forms stronger pairs with guanine, enhanced termination at this site. .rho.-Independent termination was not altered by replacing uracil with 5-bromouracil. There are 2 major .rho.-dependent termination sites on the T3 DNA-at 8 and 15%. The termination activity of .rho. in this system also depended on **RNA** secondary structure. The incorporation of 5-bromouracil instead of uracil into **RNA** did not alter the site specificity of .rho. action but .rho. was rendered inactive when cytosine was replaced by 5-bromocytosine. In contrast, replacement of GTP with ITP in the reaction increased .rho.-dependent inhibition of **RNA** synthesis, caused production of heterogeneous-sized transcripts and stimulated .rho.-mediated ATP hydrolysis. The .rho.-associated ATPase activity, in the presence of isolated T3 **RNA**, was also stimulated by **inosine** substitution.

The temperature-sensitive .rho. isolated from rho 15 mutant of E. coli, which does not terminate transcription in the presence of the common rNTP [phage], was active when GTP was replaced with ITP. Strongly paired G .times. C-rich regions in **RNA** stem-loop structures or **RNA** .cntdot. DNA hybrids are essential for .rho.-independent termination, whereas .rho.-dependent termination requires weakly paired cytosine residues for its action.

1979

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Set      Items   Description
S1        3859   RNA AND POLYMERAS? AND ANALOG? AND PY<2000
S2          30   S1 AND (2 (W) THIOCYTIDINE OR PYRROLOPYRIMIDINE OR INOSINE
               OR 2 (W)THIOTHYMIDINE OR 2 (W) AMINOADENOSIN OR 2 (W) THIOCYT-
               IDINE)
S3          27   RD (unique items)
? s s1 not s2
             3859  S1
               30  S2
      S4     3829  S1 NOT S2
? s s4 and mutant?
             3829  S4
           359064  MUTANT?
      S5      334  S4 AND MUTANT?
? s s5 and polymeriz?
              334  S5
            37292  POLYMERIZ?
      S6        9  S5 AND POLYMERIZ?
? rd
...completed examining records
      S7        7  RD (unique items)
? t s7/3,ab/all

 7/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08984677   96387193   PMID: 8794733
   Biochemical analysis of catalytically crucial aspartate mutants of
human immunodeficiency virus type 1 reverse transcriptase.
  Kaushik N; Rege N; Yadav PN; Sarafianos SG; Modak MJ; Pandey VN
  Department  of Biochemistry and Molecular Biology, UMD-New Jersey Medical
School, Newark 07103, USA.
  Biochemistry (UNITED STATES)  Sep 10 1996,  35  (36)  p11536-46,
ISSN 0006-2960  Journal Code: A0G
  Contract/Grant No.: CA72821, CA, NCI
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  In order to clarify the role(s) of the individual member of the
carboxylate triad in the catalytic mechanism of human immunodeficiency
virus type 1 (HIV-1) reverse transcriptase, we carried out site-directed
mutagenesis of D185, D186, and D110, followed by the extensive
characterization of the properties of the individual mutant enzymes.
We find that all three residues participate at or prior to the chemical
step of bond formation. The incorporation pattern seen with
phosphorothioate analogs of dNTP on both RNA-DNA and DNA-DNA
template-primers indicated that D186 may be the residue that coordinates
with the alpha-phosphate group of dNTP in the transition-state ternary
complex. Further support for the role assigned to D186 was obtained by
examination of the ability of the individual carboxylate mutants to
catalyze the reverse of the polymerase reaction (pyrophosphorolysis).
Mutants of D185 exhibited near-normal pyrophosphorolysis activity,
while those of D186 were completely devoid of this activity. Thus, D185
appears to participate only in the forward reaction, probably required for
the generation of nucleophile by interacting with the 3'-OH of the primer
terminus, while D186 seems to be involved in both the forward and the
reverse reactions, presumably by participating in the pentavalent
intermediate transition state. Lack of any elemental effects during
polymerization with mutant enzymes of residue D110, together
with their inability to catalyze pyrophosphorolysis, suggest its probable
participation in the metal-coordinated binding to the beta-gamma-phosphate
of dNTP or PPi in the forward and reverse reactions, respectively. A
molecular model of the ternary complex based on these results is also
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presented.

7/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08868209 96214911 PMID: 8617758
Human immunodeficiency virus reverse transcriptase. Functional **mutants** obtained by random mutagenesis coupled with genetic selection in Escherichia coli.
Kim B; Hathaway TR; Loeb LA
Joseph Gottstein Memorial Cancer Research Laboratory, Department of Pathology, Box 357705, University of Washington, Seattle, Washington 98195-7705, USA.
Journal of biological chemistry (UNITED STATES) Mar 1 **1996**, 271 (9) p4872-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: 5T32-CA-09437-13, CA, NCI; R35-CA-39903, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We describe catalytically active **mutants** of HIV RT (human immunodeficiency virus reverse transcriptase) generated by random sequence mutagenesis and selected in Escherichia coli for ability to complement the temperature-sensitive phenotype of a DNA **polymerase** I (Pol Its) **mutant** . We targeted amino acids Asp-67 through Arg-78 in HIV RT, which form part of the beta3-beta4 flexible loop and harbor many of the currently known mutations that confer resistance to nucleoside **analogs**. DNA sequencing of 109 selected **mutants** that complement the Pol Its phenotype revealed substitutions at all 12 residues targeted, indicating that none of the wild-type amino acids is essential. However, single mutations were not observed at Trp-71, Arg-72, and Arg-78, consistent with evolutionary conservation of these residues among viral RTs and lack of variation at these positions among isolates from patients. The mutations we recovered included most of those associated with drug resistance as well as previously unidentified mutations. Purification and assay of 14 **mutant** proteins revealed correlation between their DNA-dependent DNA **polymerize** activity in vitro and ability to complement the Pol Its phenotype. Activity of several **mutants** was resistant to 3'-azidothymidine triphosphate. We conclude that random sequence mutagenesis coupled with positive genetic selection in E. coli yields large numbers of functional HIV RT **mutants**. Among these are less active variants which are unlikely to be isolated from HIV-infected individuals and which will be informative of the roles of individual amino acids in the catalytic functions of the enzyme.

7/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08735191 95224020 PMID: 7535930
Mutated K65R recombinant reverse transcriptase of human immunodeficiency virus type 1 shows diminished chain termination in the presence of 2',3'-dideoxycytidine 5'-triphosphate and other drugs.
Gu Z; Arts EJ; Parniak MA; Wainberg MA
McGill University AIDS Center, Lady Davis Institute-Jewish General Hospital, Montreal, QC, Canada.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Mar 28 **1995**, 92 (7) p2760-4, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A lysine-to-arginine substitution at amino acid 65 (K65R) in human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) is

associated with resistance to 2',3'-dideoxycytidine (ddC), 2',3'-dideoxyinosine (ddI), and the (-) enantiomer of 2',3'-dideoxy-3'-thiacytidine (3TC). To further characterize the molecular basis of such resistance, we expressed the pp6/p51 heterodimer of wild-type RT, K65R mutated RT, and a doubly mutated (K65R/M184V) RT in Escherichia coli and assessed the characteristics of nucleotide incorporation and chain termination in cell-free reverse transcription reactions in the presence and absence of various nucleoside triphosphate **analogs** . These reactions employed a HIV **RNA** template (HIV-PBS) that contained the primer binding sequence (PBS) and the U5 and R regions of HIV-1 genomic **RNA** and an oligodeoxynucleotide (dPR) complementary to the HIV-1 PBS as primer. The K65R and K65R/M184V RTs showed significantly decreased chain-termination effects during **polymerization** with the 5'-triphosphates of ddC, 3TC, 2',3'-dideoxyadenosine, and AZT (3'-azido-3'-deoxythymidine) in comparison with wild-type RT. Detailed analysis with ddCTP and wild-type RT revealed that chain termination occurred at all guanines in the **RNA** template. However, the frequency of dideoxynucleoside triphosphate (ddNTP)-induced chain termination was decreased at certain guanines but not others in reactions catalyzed by K65R RT. Both the K65R **mutant** RT and wild-type RT had similar processive activity. These results indicate that decreased chain termination of K65R RT in the presence of ddNTPs is consistent with data obtained in viral replication assays.

7/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08584929 95188201 PMID: 7533664
Cytotoxicity, metabolism, and mechanisms of action of 2',2'-difluorodeoxyguanosine in Chinese hamster ovary cells.
Gandhi V; Mineishi S; Huang P; Chapman AJ; Yang Y; Chen F; Nowak B; Chubb S; Hertel LW; Plunkett W
Department of Clinical Investigation, University of Texas M.D. Anderson Cancer Center, Houston 77030.
Cancer research (UNITED STATES) Apr 1 **1995**, 55 (7) p1517-24,
ISSN 0008-5472 Journal Code: CNF
Contract/Grant No.: CA 28596, CA, NCI; CA 57629, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The emerging clinical success of gemcitabine (2',2'-difluorodeoxycytidine) stimulated interest in the synthesis and evaluation of purine congeners. The cytotoxicity, metabolism, and mechanisms of action of the lead candidate, 2',2'-difluorodeoxyguanosine (dFdGuo), were studied in Chinese hamster ovary cells. Unlike the natural nucleoside deoxyguanosine (dGuo), dFdGuo was not a substrate for purine nucleoside phosphorylase. Wild-type Chinese hamster ovary cells and a **mutant** line deficient in deoxycytidine (dCyd) kinase were similarly affected by dFdGuo (50% inhibitory concentration, 7.5 and 6.5 microM, respectively), suggesting that unlike gemcitabine, dCyd kinase was not responsible for activation of dFdGuo. This was further confirmed by separation of nucleoside kinases (adenosine kinase, dGuo kinase, and dCyd kinase) of Chinese hamster ovary cells on DEAE-cellulose column chromatography. The kinase activity that phosphorylated dGuo also converted dFdGuo to its monophosphate, suggesting that dGuo kinase activated dFdGuo. Consistent with this result, coincubation with dGuo spared the dFdGuo-mediated toxicity; however, addition of up to 10 mM dCyd did not reverse the toxicity of dFdGuo. Intracellularly, dFdGuo was phosphorylated to its mono-, di-, and triphosphates; dFdGuo triphosphate (dFdGTP) was the major metabolite and accumulated to 45 microM after a 6-h incubation with 30 microM dFdGuo. The elimination of dFdGTP was monophasic with a t1/2 of about 6 h. Deoxynucleotides were decreased in cells incubated with dFdGuo, suggesting that ribonucleotide reductase was inhibited. dATP, which decreased 78%

after a 4-h incubation with 30 microM dFdGuo, was most affected. dFdGuo was a potent inhibitor of DNA synthesis. Extension of a DNA primer over a defined template in the presence of dFdGTP revealed that dFdGTP was a good substrate for incorporation opposite C sites of the template by DNA **polymerase** alpha. dFdGTP incorporation caused DNA **polymerase** alpha to pause after the **polymerization** of one additional deoxynucleotide. This pattern of inhibition, which is shared by gemcitabine, distinguishes 2',2'-difluoronucleosides from arabinosylnucleosides which halt primer extension at the incorporation site. dGTP competed effectively with dFdGTP for incorporation by DNA **polymerase** alpha. The unique activation requirements and patterns of inhibition of DNA synthesis distinguish this promising new antimetabolite from other nucleoside **analogues**.

7/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07770541 91153326 PMID: 1847871
Lys631 residue in the active site of the bacteriophage T7 **RNA polymerase**. Affinity labeling and site-directed mutagenesis.
Maksimova TG; Mustayev AA; Zaychikov EF; Lyakhov DL; Tunitskaya VL; Akbarov AKh; Luchin SV; Rechinsky VO; Chernov BK; Kochetkov SN
Limnological Institute, Siberian Division of the USSR Academy of Sciences, Irkutsk.
European journal of biochemistry (GERMANY) Feb 14 **1991**, 195 (3) p841-7, ISSN 0014-2956 Journal Code: EMZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A highly selective affinity labeling of T7 **RNA polymerase** with the o-formylphenyl ester of GMP and [alpha-32P]UTP was carried out. The site of the labeling was located using limited cleavages with hydroxylamine, bromine, N-chlorosuccinimide and cyanogene bromide and was identified as the Lys631 residue. Site-directed mutagenesis using synthetic oligonucleotides was used to substitute Lys631 by a Gly, Leu or Arg residue. Kinetic studies of the purified **mutant** enzymes showed alterations of their **polymerizing** activity. For the Lys----Gly **mutant** enzyme, anomalous template binding was observed.

7/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07705263 92250580 PMID: 1315753
Point mutations which drastically affect the **polymerization** activity of encephalomyocarditis virus **RNA**-dependent **RNA polymerase** correspond to the active site of Escherichia coli DNA **polymerase** I.
Sankar S; Porter AG
Institute of Molecular and Cell Biology, National University of Singapore, Kent Ridge, Crescent.
Journal of biological chemistry (UNITED STATES) May 15 **1992**, 267 (14) p10168-76, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The inhibitor sensitivity and functional domains of recombinant encephalomyocarditis (EMC) virus **RNA**-dependent **RNA polymerase** (3Dpol) have been extensively analyzed. The inhibitor profiles of EMC virus 3Dpol and Escherichia coli DNA-dependent **RNA polymerase** are distinct, and experiments with substrate **analogs** indicate that EMC virus 3Dpol lacks reverse transcriptase activity. Twenty amino acid substitutions were engineered in EMC virus 3Dpol based on

sequence alignments of viral **RNA**-dependent **RNA polymerases** that identified conserved amino acid residues within motifs. Ten out of 17 conservative substitutions within the four most conserved motifs reduced the **RNA polymerase** activity of the **mutants** to 0-6% of the activity of the wild-type enzyme, demonstrating the importance of these amino acids in the structure and/or function of EMC virus 3Dpol. Remarkably, 5 of the 10 mutations in EMC virus 3Dpol which had the most drastic effect on its **RNA polymerase** activity (D240E, S293T, N302Q, G332A, and D333E) were found to correspond to active site residues in E. coli DNA-dependent DNA **polymerase** I (Klenow). Our results reveal that a basic structural and functional framework is conserved in the most distantly related classes of nucleic acid **polymerases** and demonstrate the validity of modeling the active site of an **RNA**-dependent **RNA polymerase** on the known structure of a DNA **polymerase**.

7/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06415444 87280237 PMID: 3301854
Studies on the role of actin's N tau-methylhistidine using oligodeoxynucleotide-directed site-specific mutagenesis.
Solomon LR; Rubenstein PA
Journal of biological chemistry (UNITED STATES) Aug 15 **1987**, 262 (23) p11382-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM-33689, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The primary structure of all actins except that isolated from Naegleria gruberi contains a unique N tau-methylhistidine (MeHis) at position 73. This modified residue has been implicated as possibly being important for the post-translational processing of actin's amino terminus, the binding of actin to DNase I, and in the **polymerization** of G-actin. We have investigated the potential role of MeHis in each of these processes by utilizing site-directed mutagenesis to change His-73 of skeletal muscle actin to Arg and Tyr. Wild type and **mutant** actins were synthesized in vivo, using non-muscle cells transfected with **mutant** cDNAs, and in vitro by translating **mutant** RNAs synthesized using SP6 **RNA polymerase** in a rabbit reticulocyte lysate. We have found that actins containing Arg or Tyr at position 73 undergo amino-terminal processing, bind to DNase I-agarose, and become incorporated into the cytoskeleton of a nonmuscle cell as efficiently as wild type actin. Furthermore, using an in vitro copolymerization assay we have found that although there is no difference between the Arg **mutant** and the wild type actins, the Tyr **mutant** has a slightly greater critical concentration for **polymerization** . These results show that MeHis is not absolutely required for any of these processes.

08808371 96139538 PMID: 8585725
Inhibition of influenza virus transcription by 2'-deoxy-2'-fluoroguanosin
e.
Tisdale M; Ellis M; Klumpp K; Court S; Ford M
Wellcome Research Laboratories, Beckenham, Kent, United Kingdom.
Antimicrobial agents and chemotherapy (UNITED STATES) Nov **1995**,
39 (11) p2454-8, ISSN 0066-4804 Journal Code: 6HK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The nucleoside **analog** 2'-deoxy-2'-fluoroguanosine (2'-fluorodGuo)
is phosphorylated by cellular enzymes and reversibly inhibits influenza
virus replication in chick embryo cells within the first 4 h of infection.
RNA hybridization studies revealed that primary and secondary
transcription of influenza virus **RNA** were blocked at a compound
concentration of 10 microM, but no inhibition of cell protein synthesis was
seen even at high compound concentrations (200 microM). In vitro, the
triphosphate of 2'-fluorodGuo is a competitive inhibitor of influenza virus
transcriptase activity from disrupted virus, with a Ki of 1.0 microM. The
cellular **polymerases** DNA **polymerase** alpha and **RNA**
polymerase II were only weakly inhibited or were insusceptible to
2'-fluorodGTP. In kinetic studies with the influenza virus transcriptase,
2'-fluorodGTP, in the absence of GTP, blocked elongation of the virus
RNA chain. Similarly, by using purified ribonucleoprotein complexes
it was found that the addition of a single nucleotide of 2'-fluorodGTP to
the virus **RNA** caused chain termination, which resulted in the
blockage of further virus transcription. Furthermore, the specificity for
influenza virus transcriptase was confirmed when the transcriptase from
partially resistant virus was found to be 10-fold less susceptible to
2'-fluorodGTP (Ki = 13.1 microM).

10/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08774283 95363981 PMID: 7637014
RNA replication by respiratory syncytial virus (RSV) is directed by
the N, P, and L proteins; transcription also occurs under these conditions
but requires RSV superinfection for efficient synthesis of full-length
mRNA.
Grosfeld H; Hill MG; Collins PL
Laboratory of Infectious Diseases, National Institute of Allergy and
Infectious Disease, Bethesda, Maryland 20892-0720, USA.
Journal of virology (UNITED STATES) Sep **1995**, 69 (9) p5677-86,
ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Previously, a cDNA was constructed so that transcription by T7 **RNA**
polymerase yielded a approximately 1-kb negative-sense **analog**
of genomic **RNA** of human respiratory syncytial virus (RSV) containing
the gene for chloramphenicol acetyltransferase (CAT) under the control of
putative RSV transcription motifs and flanked by the RSV genomic termini.
When transfected into RSV-infected cells, this minigenome was "rescued," as
evidenced by high levels of CAT expression and the production of
transmissible particles which propagated and expressed high levels of CAT
expression during serial passage (P.L. Collins, M. A. Mink, and D. S. Stec,
Proc. Natl. Acad. Sci. USA, 88:9663-9667, 1991). Here, this cDNA, together
with a second one designed to yield an exact-copy positive-sense RSV-CAT
RNA antigenome, were each modified to contain a self-cleaving
hammerhead ribozyme for the generation of a nearly exact 3' end. Each cDNA
was transfected into cells infected with a vaccinia virus recombinant
expressing T7 **RNA polymerase**, together with plasmids encoding
the RSV N, P, and L proteins, each under the control of a T7 promoter. When

the plasmid-supplied template was the mini-antigenome, the minigenome was produced. When the plasmid-supplied template was the minigenome, the products were mini-antigenome, subgenomic polyadenylated mRNA and progeny minigenome. Identification of progeny minigenome made from the plasmid-supplied minigenome template indicates that the full RSV **RNA** replication cycle occurred. **RNA** synthesis required all three RSV proteins, N, P, and L, and was ablated completely by the substitution of Asn for Asp at position 989 in the L protein. Thus, the N, P, and L proteins were sufficient for the synthesis of correct minigenome and antigenome, but this was not the case for subgenomic mRNA, indicating that the requirements for **RNA** replication and transcription are not identical. Complementation with N, P, and L alone yielded an mRNA pattern containing a large fraction of molecules of incomplete, heterogeneous size. In contrast, complementation with RSV (supplying all of the RSV gene products) yielded a single discrete mRNA band. Superinfection with RSV of cells staging N/P/L-based **RNA** synthesis yielded the single discrete mRNA species. Some additional factor supplied by RSV superinfection appeared to be involved in transcription, the most obvious possibility being one or more additional RSV gene products.

10/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08769551 95281586 PMID: 7539140

NusA interferes with interactions between the nascent **RNA** and the C-terminal domain of the alpha subunit of **RNA polymerase** in Escherichia coli transcription complexes.

Liu K; Hanna MM

Department of Botany and Microbiology, University of Oklahoma, Norman 73019, USA.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) May 23 **1995**, 92 (11) p5012-6, ISSN 0027-8424 Journal Code: PV3

Contract/Grant No.: RO1 GM47493, GM, NIGMS

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The effects of NusA on the **RNA polymerase** contacts made by nucleotides at internal positions in the nascent **RNA** in Escherichia coli transcription complexes were analyzed by using the photocrosslinking nucleotide **analog** 5-[(4-azidophenacyl) thio]-UMP. It was placed at nucleotides between +6 and +15 in **RNA** transcribed from the phage lambda PR' promoter. Crosslinks of **analog** in these positions in RNAs which contained either 15, 28, 29, or 49 nt were examined. Contacts between the nascent **RNA** and proteins in the transcription complex were analyzed as the **RNA** was elongated, by placing the crosslinker nearest the 5' end of the **RNA** 10, 23, 24, or 44 nt away from the 3' end. The beta or beta' subunit of **polymerase** , and NusA when added, were contacted by **RNA** from 15 to 49 nt long. When the upstream crosslinker was 24 nt from the 3" end of the **RNA** (29-nt **RNA**), alpha was also contacted in the absence of NusA. The addition of NusA prevented **RNA** crosslinking to alpha. When the crosslinker was 44 nt from the 3' end (49-nt **RNA**), alpha crosslinks were still observed, but crosslinks to beta or beta' and NusA were greatly diminished. **RNA** crosslinking to alpha, and loss of this crosslink when NusA was added, was observed in the presence of NusB, NusE, and NusG and when transcription was carried out in the presence of an E. coli S100 cell extract. Peptide mapping localized the **RNA** interactions to the C-terminal domain of alpha.

10/3,AB/28 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08768969 95270597 PMID: 7751289
Effector-mediated stimulation of ATPase activity by the sigma 54-dependent transcriptional activator FHLA from Escherichia coli.
Hopper S; Bock A
Lehrstuhl fur Mikrobiologie, Universitat Munchen, Germany.
Journal of bacteriology (UNITED STATES) May **1995**, 177 (10) p2798-803, ISSN 0021-9193 Journal Code: HH3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The FHLA protein is the transcriptional regulator of the genes of the formate regulon from Escherichia coli. The protein shares homology with the sigma 54-dependent regulators of the NTRC family in the central and C-terminal domains but differs in possessing an extended N terminus lacking the aspartate residue which is the site of phosphorylation. Purified FHLA displays intrinsic ATPase activity which is stimulated weakly by formate and DNA. The presence of both formate and DNA carrying the upstream regulatory sequence to which FHLA binds leads to a large increase in the rate of ATP hydrolysis. Hypophosphite, a structural **analog** of formate, and azide, a transition state **analog** of formate, also stimulate ATPase activity, supporting the conclusion that formate is a direct ligand of FHLA. Half-maximal saturation of FHLA with formate took place at around 5 mM, and half-maximal saturation with target DNA took place at around 50 nM. The stimulation of ATPase activity by formate was conferred by a decrease in the apparent Km for ATP, whereas the effect of the DNA binding site also affected the Kcat of the reaction. The other nucleoside triphosphates, GTP, UTP, and CTP, competed with ATP cleavage by FHLA, suggesting at least their binding to FHLA. The specific ATPase activity of FHLA was dependent on the concentration of FHLA in the assay, especially in the presence of DNA and formate. Direct liganding of the effector, therefore, leads to the same consequence as phosphorylation for the NTRC-type regulators, namely, stimulation of ATPase activity.

10/3,AB/29 (Item 29 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08763953 95119054 PMID: 7819262
Tests of a model of specific contacts in T7 **RNA polymerase** -promoter interactions.
Schick C; Martin CT
Program in Molecular and Cellular Biology, University of Massachusetts, Amherst 01003.
Biochemistry (UNITED STATES) Jan 17 **1995**, 34 (2) p666-72, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The T7, T3, and SP6 **RNA polymerases** represent a highly homologous family of enzymes that recognize similarly homologous promoter DNA sequences. Despite these similarities, the enzymes are highly specific for their respective promoters. Studies of mutant **RNA polymerases** have linked a specific amino acid residue in the protein to recognition of bases at positions -11 and -10 in the promoter [Raskin, C. A., et al. (1992) J. Mol. Biol. 228, 506-515]. In kinetic analyses of transcription from synthetic promoters containing base-**analog** substitutions, we have recently shown that at positions -11 and -10 of the T3 promoter, T3 **RNA polymerase** recognizes functional groups along the nontemplate strand wall of the major groove [Schick, C., & Martin, C. T. (1993) Biochemistry 32, 4275-4780]. We now extend these studies to the homologous region of the T7 promoter. The results confirm extrapolations from the T3 system and show that T7 **RNA polymerase** recognizes corresponding functional groups at positions -11 and -10 of the T7 promoter. The results are consistent with a direct

readout model for recognition of these bases [Raskin, C. A., et al. (1992) J. Mol. Biol., 228, 506-515], in which the 6-carbonyl and 7-imino groups of the nontemplate guanine at position -11 and the 6-amino group of the nontemplate adenine at position -10 of the T7 promoter are directly involved in binding. The results further support an overall model for promoter recognition in which the enzyme binds to one face of the duplex DNA in this upstream region of the promoter.

10/3,AB/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08561967 95343550 PMID: 7618275

RNA transcripts derived from a cloned full-length copy of the feline calicivirus genome do not require VpG for infectivity.

Sosnovtsev S; Green KY

Laboratory of Infectious Diseases, National Institute of Allergies and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.

Virology (UNITED STATES) Jul 10 **1995**, 210 (2) p383-90, ISSN 0042-6822 Journal Code: XEA

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Feline calicivirus (FCV) is a positive-strand, nonenveloped **RNA** virus in the family Caliciviridae. A cDNA library of the Urbana (URB) strain of FCV was generated and the sequence of the genome was determined from overlapping clones except for 13 bases from the 5'-end. The 5'-end sequence was identified by analysis of clones derived by RT-PCR across the ligated 5'- and 3'-ends of the **RNA** genome. A full-length cDNA clone of the **RNA** genome of the URB strain was constructed and placed downstream of the T7 **RNA polymerase** promoter and **RNA** transcripts generated in vitro from this clone were infectious when introduced into feline kidney cells. A virus-encoded genome-linked protein, VpG, which is considered to be essential for infectivity of wild-type genomic FCV **RNA**, was not required for the initiation of FCV infection by the synthetic transcripts. However, the addition of a cap structure **analog** (m7G(5')ppp(5')G) during in vitro transcription of the synthetic **RNA** was necessary for successful virus recovery. Two silent mutations engineered into the full-length clone were identified in the genomic **RNA** from recovered progeny virus. This system of introducing site-specific genetic changes into the genome of feline calicivirus and the recovery of infectious mutant viruses will enable studies related to the molecular basis for replication, growth restriction, and pathogenicity of this and other members of the Caliciviridae.

10/3,AB/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08477555 95193238 PMID: 7886944

In vitro transcription of the double-stranded **RNA** bacteriophage phi 6 is influenced by purine NTPs and calcium.

Ojala PM; Bamford DH

Department of Genetics, University of Helsinki, Finland.

Virology (UNITED STATES) Mar 10 **1995**, 207 (2) p400-8, ISSN 0042-6822 Journal Code: XEA

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The double-stranded **RNA** bacteriophage phi 6 contains a virion-associated **RNA**-dependent **RNA polymerase** complex. Removal of the virus envelope and the nucleocapsid surface protein, P8, reveals a nucleocapsid core particle (proteins P1, P2, P4, P7) which is the

viral **polymerase** complex, capable of synthesizing **RNA** strands of positive polarity. The in vitro plus strand synthesis (transcription) reaction of the particle obtained from the mature virion was optimized and its activation and inactivation were investigated. Purine nucleoside triphosphates (NTPs), binding to a low-affinity binding site in the **polymerase** complex, activated plus strand synthesis. GTP was the preferred NTP, but dGTP, ddGTP, and the noncleavable **analog** GMP-PCP could also switch on transcription. This NTP-binding site is probably different from that of the unspecific viral NTPase found in protein P4 and also from that of the rNTP-specific **RNA polymerase** active site. Binding of purine NTPs was sufficient for the switch-on; hydrolysis of the NTP was not required. Besides nucleotides, divalent cations had an effect on phi 6 in vitro plus strand synthesis. Magnesium ions are required for the activity but calcium ions inhibit the reaction. Manganese ions are shown to dissipate the effect of magnesium and calcium ions, leading to uncontrolled, exceptionally high level plus strand synthesis.

10/3,AB/32 (Item 32 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08476807 95191018 PMID: 7884888

Functional cDNA clones of the human respiratory syncytial (RS) virus N, P, and L proteins support replication of RS virus genomic **RNA analogs** and define minimal trans-acting requirements for **RNA** replication.

Yu Q; Hardy RW; Wertz GW
Department of Microbiology, University of Alabama, School of Medicine, Birmingham 35294.

Journal of virology (UNITED STATES) Apr **1995**, 69 (4) p2412-9, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: AI12464, AI, NIAID; AI20181, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The **RNA**-dependent **RNA polymerase** of human respiratory syncytial (RS) virus was expressed in a functional form from a cDNA clone. Coexpression of the viral **polymerase** (L) protein, phosphoprotein (P), and nucleocapsid (N) protein allowed us to develop a system for expression and recovery of replicable RS virus **RNA** entirely from cDNA clones. cDNA clones of the N, P, and L genes were constructed in pGEM-based expression plasmids and shown to direct expression of the appropriate polypeptides. Two types of RS virus genomic **RNA analogs** were expressed from an intracellular transcription plasmid that directed the synthesis of RNAs with defined 5' and 3' ends. One **analog** included the authentic 5' and 3' termini of the genome, and the second contained the authentic 5' terminus and its complement at the 3' terminus as found in copyback defective interfering RNAs of other negative-strand **RNA** viruses. Both types of genomic **analogs** were encapsidated and replicated in cells expressing the RS virus N, P, and L proteins. Omission of any of the three viral proteins abrogated replication, thereby defining the N, P, and L proteins as the minimal trans-acting proteins required for **RNA** replication. This system has the advantages that expression occurs at a level sufficient to allow direct biochemical analysis of the products of **RNA** replication and that neither the use of reporter genes nor wild-type RS helper virus is required. These features allow analysis of both cis- and trans-acting factors involved in the control of replication of RS virus **RNA**.

10/3,AB/33 (Item 33 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08467674 95156588 PMID: 7853496

Lentivirus Tat proteins specifically associate with a cellular protein kinase, TAK, that hyperphosphorylates the carboxyl-terminal domain of the large subunit of **RNA polymerase** II: candidate for a Tat cofactor.

Herrmann CH; Rice AP

Division of Molecular Virology, Baylor College of Medicine, Houston, Texas 77030-3498.

Journal of virology (UNITED STATES) Mar **1995**, 69 (3) p1612-20, ISSN 0022-538X Journal Code: KCV

Contract/Grant No.: AI08663, AI, NIAID; AI25308, AI, NIAID; U01 AI30243, AI, NIAID

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Efficient replication of human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) requires the virus transactivator proteins known as Tat. In order to understand the molecular mechanisms involved in Tat transactivation, it is essential to identify the cellular target(s) of the Tat activation domain. Using an in vitro kinase assay, we previously identified a cellular protein kinase activity, Tat-associated kinase (TAK), that specifically binds to the activation domains of Tat proteins. Here it is demonstrated that TAK fulfills the genetic criteria established for a Tat cofactor. TAK binds in vitro to the activation domains of the Tat proteins of HIV-1 and HIV-2 and the distantly related lentivirus equine infectious anemia virus but not to mutant Tat proteins that contain nonfunctional activation domains. In addition, it is shown that TAK is sensitive to dichloro-1-beta-D-ribofuranosylbenzimidazole, a nucleoside **analog** that inhibits a limited number of kinases and is known to inhibit Tat transactivation in vivo and in vitro. We have further identified an in vitro substrate of TAK, the carboxyl-terminal domain of the large subunit of **RNA polymerase** II. Phosphorylation of the carboxyl-terminal domain has been proposed to trigger the transition from initiation to active elongation and also to influence later stages during elongation. Taken together, these results imply that TAK is a very promising candidate for a cellular factor that mediates Tat transactivation.

10/3,AB/34 (Item 34 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08443750 95065720 PMID: 7975272

Reverse misreading of a GC doublet by the modified T7 DNA **polymerase**, Sequenase.

Odagiri T

Department of Virology, Jichi Medical School, Tochigi, Japan.

Virus genes (UNITED STATES) Jul **1994**, 8 (3) p271-4, ISSN 0920-8569 Journal Code: XEI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

In nucleotide sequencing of the cDNA of the influenza virus PB2 **polymerase** gene by the dideoxy method using a modified T7 DNA **polymerase** , Sequenase, the sequence of the promoter region, 5'-AGCGAAAGCAGG, was shown to be misread as 5'-AGCGAAACGAGG, i.e., a GC doublet at positions 8 and 9 was read in reverse. This misreading was also found both when the sequence of BsmI restriction site upstream from the PB2 promoter sequence was exchanged by that of the promoter of T7 **RNA polymerase** and when the downstream region was substituted with the nonstructural (NS) protein gene. These results indicated that the misreading by Sequenase was attributed specifically to the PB2 promoter region, independent of the upstream and downstream sequences. The misreading, however, did not occur when dGTP in the labeling mixture was substituted with another nucleotide **analog**, dITP. Furthermore, the

reversion did not occur in the NS gene promoter region, where the nucleotide sequence was 5'-AGCAAAAGCAGG. Since the nucleotide difference between the PB2 and NS promoter regions was only at the fourth residue, i.e., G for PB2 and A for PB2 and A for NS, the G residue followed by a triplet AAA in the PB2 promoter region was suggested to be a signal responsible for the misreading by Sequenase T7 DNA **polymerase**. The findings warns of possible misreading in determining DNA sequences, in addition to compression of the sequencing ladder.

10/3,AB/35 (Item 35 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08442158 95045524 PMID: 7957189
Evidence for a pyrimidine-nucleotide-specific initiation site (the i site) on Escherichia coli **RNA polymerase** . Proximity relationship with the inhibitor binding domain.
Reddy PS; Chatterji D
Centre for Cellular and Molecular Biology, Hyderabad, India.
European journal of biochemistry (GERMANY) Oct 15 **1994**, 225 (2) p737-45, ISSN 0014-2956 Journal Code: EMZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Escherichia coli **RNA polymerase** has two sites, the i and i + 1, for the binding of the first two substrates. The i site is template- and Mg(2+)-independent and purine-nucleotide-specific, whereas the i + 1 site is template- and Mg(2+)-dependent and shows no nucleotide preference. The specificity of the i site for purine nucleotides is well in accord with the fact that most promoters initiate with a purine nucleotide. But there are a few promoters that initiate with a pyrimidine nucleotide. Dinucleotide synthesis at these promoters is completely inhibited by rifampicin. Earlier studies have failed to identify an i site for pyrimidine nucleotides. In this paper, using a fluorescent **analog** of UTP, namely uridine 5'-[gamma-(5-sulfonic acid)naphthylamidate]-triphosphate, abbreviated as UTP[AmNS], we are able to show its binding to **RNA polymerase**, with a Kd of 0.8 microM, in the absence of Mg2+ and template. This suggests the presence of an i pyrimidine nucleotide site. The fact that UTP-[AmNS] is capable of initiating **RNA** synthesis from the i site is further evidenced by the abortive transcription analyses at the lac promoter. Fluorescence titration studies performed in the presence and absence of purine initiator molecules indicate that this site is different from the i purine site. Scatchard analysis of the above data indicates the presence of a single binding site for UTP[AmNS] in the absence of Mg2+. Moreover UTP[AmNS] binds to the core enzyme with a Kd of 3.0 microM implying that, unlike the i purine nucleotide site, the sigma protein confers a tighter binding of UTP-[AmNS] to the low-Kd site. Forster's energy transfer measurements using UTP[AmNS] as the donor and rifampicin as the acceptor have been used for estimation of the distance of the i pyrimidine nucleotide site from the rifampicin site. From these measurements, we infer that there is no direct interference of rifampicin with the first phosphodiester bond between two pyrimidine nucleotides.

10/3,AB/36 (Item 36 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08428349 94278492 PMID: 7516580
Structures of ternary complexes of rat DNA **polymerase** beta, a DNA template-primer, and ddCTP.
Pelletier H; Sawaya MR; Kumar A; Wilson SH; Kraut J
Department of Chemistry, University of California, San Diego 92093-0317.
Science (UNITED STATES) Jun 24 **1994**, 264 (5167) p1891-903, ISSN 0036-8075 Journal Code: UJ7

Contract/Grant No.: CA17374, CA, NCI; ES06839, ES, NIEHS; GM10928, GM, NIGMS
Comment in Science. 1994 Dec 23;266(5193) 2022-5
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Two ternary complexes of rat DNA **polymerase** beta (pol beta), a DNA template-primer, and dideoxycytidine triphosphate (ddCTP) have been determined at 2.9 A and 3.6 A resolution, respectively. ddCTP is the triphosphate of dideoxycytidine (ddC), a nucleoside **analog** that targets the reverse transcriptase of human immunodeficiency virus (HIV) and is at present used to treat AIDS. Although crystals of the two complexes belong to different space groups, the structures are similar, suggesting that the **polymerase** -DNA-ddCTP interactions are not affected by crystal packing forces. In the pol beta active site, the attacking 3'-OH of the elongating primer, the ddCTP phosphates, and two Mg2+ ions are all clustered around Asp190, Asp192, and Asp256. Two of these residues, Asp190 and Asp256, are present in the amino acid sequences of all **polymerases** so far studied and are also spatially similar in the four **polymerases**--the Klenow fragment of Escherichia coli DNA **polymerase** I, HIV-1 reverse transcriptase, T7 **RNA polymerase** , and rat DNA pol beta--whose crystal structures are now known. A two-metal ion mechanism is described for the nucleotidyl transfer reaction and may apply to all **polymerases**. In the ternary complex structures analyzed, pol beta binds to the DNA template-primer in a different manner from that recently proposed for other **polymerase**-DNA models.

10/3,AB/37 (Item 37 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08380349 94230437 PMID: 7513701

Inhibitors of transcription such as 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole and isoquinoline sulfonamide derivatives (H-8 and H-7) promote dephosphorylation of the carboxyl-terminal domain of **RNA polymerase** II largest subunit.

Dubois MF; Nguyen VT; Bellier S; Bensaude O
Laboratoire de Genetique Moleculaire, URA CNRS 1302, Ecole Normale Superieure, Paris, France.

Journal of biological chemistry (UNITED STATES) May 6 **1994**, 269 (18) p13331-6, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The **RNA polymerase** IIO and IIA differ by the extent of phosphorylation in the carboxyl-terminal domain (CTD) of the largest subunit. It has been proposed that the IIA form of **RNA polymerase** II interacts with the promoter to form a stable preinitiation complex whereas the IIO form would be generated upon entry into initiation of transcription. Phosphorylation of the CTD might be required to release the interaction between the **polymerase** and the promoter binding factors. In this paper, we show that in the presence of actinomycin D, the phosphorylated IIO form accumulates. In contrast, the dephosphorylated IIA form accumulates while the amount of phosphorylated IIo form decreases in cells treated with CTD-kinase inhibitors such as the nucleoside **analog** , 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole or the isoquinoline sulfonamide derivatives H-7* or H-8. These changes are fast and suggest a very rapid phosphate turnover on the CTD. Transcription is inhibited in intact cells by drug concentrations that are effective in altering CTD phosphorylation, although no causal relationship is established yet. These effects do not concern other cellular functions such as protein synthesis. Thus isoquinoline sulfonamide derivatives might be helpful to further dissect the role of CTD phosphorylation in

transcription.

10/3,AB/38 (Item 38 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08296507 95075651 PMID: 7984420
Transcription of satellite 2 DNA from the newt is driven by a snRNA type of promoter.
Coats SR; Zhang Y; Epstein LM
Institute of Molecular Biophysics, Florida State University, Tallahassee 32306.
Nucleic acids research (ENGLAND) Nov 11 **1994**, 22 (22) p4697-704, ISSN 0305-1048 Journal Code: O8L
Contract/Grant No.: GM 38791, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The transcriptional promoter of satellite 2 from the eastern newt, Notophthalmus viridescens, was analyzed by assaying the activity of deleted or mutated satellite 2 clones in Xenopus laevis oocytes. Two elements in the promoter were found to be important for transcription. These elements have sequences that are similar to the sequences of the octamer and the proximal sequence element of vertebrate snRNA genes transcribed by **RNA polymerase** II. Furthermore, the organization of these elements and their respective roles in transcription are the same as their organization and roles in the snRNA genes. To further investigate the relationship between the satellite 2 and snRNA gene promoters, the ability of the satellite 2 promoter to drive transcription of a true snRNA gene was tested. The satellite 2 promoter initiated transcription of the Xenopus U1b2 snRNA gene as efficiently as the native U1b2 promoter, and the 3' ends of the resulting U1b2 transcripts were accurately formed. This latter result confirms that the satellite 2 promoter is a functional **analog** of the snRNA promoter, since 3'-end formation of snRNA genes transcribed by **RNA polymerase** II requires that transcription be initiated from a compatible promoter. The structural and functional similarities between the satellite 2 and the snRNA gene promoters suggest that these elements are evolutionarily related. These findings were used to extend a previously proposed model concerning the nature and derivation of satellite 2.

10/3,AB/39 (Item 39 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08158977 94242414 PMID: 8185933
Inhibition of germinal vesicle breakdown in bovine oocytes by 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole (DRB).
Farin CE; Yang L
Department of Animal Science, North Carolina State University, Raleigh 27695-7621.
Molecular reproduction and development (UNITED STATES) Mar **1994**, 37 (3) p284-92, ISSN 1040-452X Journal Code: AN7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
5,6-Dichloro-1-beta-D-ribofuranosyl-benzimidazole (DRB) is an **analog** of the nucleoside adenosine that has been used to inhibit transcription in a variety of cell types. The present studies were designed to evaluate the ability of DRB to block germinal vesicle breakdown (GVBD) in bovine oocytes matured in vitro and to characterize culture conditions required for DRB-mediated arrest of meiosis. Administration of DRB (60-90 microM) at 2-3 h intervals during culture of COC blocked GVBD in approximately 70 percent of oocytes. The inhibitory effect of DRB was reversible and required the presence of cumulus cells. Treatment with DRB

was associated with a 57% decrease in 3H-uridine incorporation into total COC **RNA** and a 90.8% decrease into mRNA but did not affect the incorporation of 3H-leucine into COC proteins. The ability of DRB to arrest meiosis was significantly compromised if supplemental gonadotropin preparations were absent from the maturation media. Gonadotropin-induced GVBD as well as cumulus cell expansion was blocked by treatment with DRB but not with adenosine. GVBD in cultured bovine COC was initially inhibited and then stimulated when supplemental gonadotropin preparations were included in the culture media. DRB treatment in the presence of gonadotropin supplementation blocked the stimulatory effect of gonadotropins on GVBD. In conclusion, DRB can be used to arrest GVBD in bovine COC in a specific and reversible manner. The data support the hypothesis that gene transcription is required for the stimulatory phase of gonadotropin-mediated GVBD in cultured bovine COC.

10/3,AB/40 (Item 40 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08113949 94147985 PMID: 8313884
Transcription initiation by **RNA polymerase** II does not require hydrolysis of the beta-gamma phosphoanhydride bond of ATP.
Timmers HT
Laboratory for Physiological Chemistry, Utrecht University, The Netherlands.
EMBO journal (ENGLAND) Jan 15 **1994**, 13 (2) p391-9, ISSN 0261-4189 Journal Code: EMB
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
When transcription by **RNA polymerase** II from the major-late (ML) promoter was studied with purified basal transcription factors, it was observed that transcription from negatively-supercoiled ML templates did not require transcription factor IIH (TFIIH). Addition of the basal factor TFIIE was highly stimulatory, but not absolutely required for this reaction. In contrast, transcription from relaxed or linear ML templates required both TFIIE and TFIIH. Adenylylimidodiphosphate (AMP-PNP), an ATP **analog** with a non-hydrolyzable beta-gamma phosphoanhydride bond, could support **RNA** synthesis from supercoiled templates, but not from linear templates. Since AMP-PNP cannot act as a cofactor for the DNA helicase activity of TFIIH, this finding independently supported the conclusion that TFIIH is not required for transcription of negatively-supercoiled templates. Taken together, these data indicate that the ATP-dependent step in transcription initiation by **RNA polymerase** II is caused by a requirement for the ATP-dependent helicase activity of the basal factor TFIIH. The experiments also show that transcription initiation by **RNA polymerase** II does not require hydrolysis of the beta-gamma phosphoanhydride bond of ATP per se.

10/3,AB/41 (Item 41 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08094367 93323109 PMID: 8331654
Bacteriophage T7 **RNA polymerase** . 19F-nuclear magnetic resonance observations at 5-fluorouracil-substituted promoter DNA and **RNA** transcript.
Rastinejad F; Lu P
Department of Biochemistry and Biophysics, University of Pennsylvania, Philadelphia 19104.
Journal of molecular biology (ENGLAND) Jul 5 **1993**, 232 (1) p105-22, ISSN 0022-2836 Journal Code: J6V
Languages: ENGLISH
Document type: Journal Article

Record type: Completed
We have substituted 5-fluorodeoxyuridine (5-FdU) in place of thymidine in defined positions along synthetic bacteriophage T7 promoter DNA sequences. None of the fluoro-substitutions in the promoter DNA sequence reduced transcription yields with T7 **RNA polymerase** significantly. Substitutions on the coding template strand reduced transcription yields when placed at +3, but not at +4. 19F-n.m.r. spectra from transcription reactions and gel analysis of transcription products show that T7 **RNA polymerase** correctly and efficiently utilizes 5-FUTP as a **RNA** substrate **analog** . The fluorine atom provides a sensitive probe for monitoring the local environment, base sequence and solvent exposure at the DNA major groove through its 19F-n.m.r. resonance. Buffer dependencies of the fluorine chemical shift and digestion patterns with DNase I suggest that the T7 promoter base-pairs near the transcription start site are distorted with a more open minor groove and less solvent accessible major groove. Previous chemical footprinting data of promoter-**polymerase** complexes yield a picture that T7 **RNA polymerase** recognizes major groove features in the region from positions -7 to -11 and minor groove features on the same side of DNA flanking both sides of this region. Consistent with this, 19F-n.m.r. observations identify two additional positions, -8 and -17, involved in promoter recognition on this side of the DNA helix. On the other hand, our observations also implicate the opposite side of the DNA helix, primarily at positions -14 and -15, as major groove recognition sites for T7 **RNA polymerase**. In addition, n.m.r. spectra from 5-FdU-substituted base-pairs -2 and -3, suggest either additional interactions on the same side of the DNA helix as -14 and -15, or distortions in the DNA structure.

10/3,AB/42 (Item 42 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08036574 93275732 PMID: 7684833
Synthesis and characterization of a new photocrosslinking CTP **analog** and its use in photoaffinity labeling E. coli and T7 **RNA polymerases**.
Hanna MM; Zhang Y; Reidling JC; Thomas MJ; Jou J
Department of Botany and Microbiology, University of Oklahoma, Norman 73019.
Nucleic acids research (ENGLAND) May 11 **1993**, 21 (9) p2073-9, ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A new photocrosslinking CTP **analog** that functioned as a substrate during transcription was synthesized and used to photoaffinity label E. coli and bacteriophage T7 **RNA polymerases**. This **analog**, 5-((4-azidophenacyl)thio) cytidine-5'-triphosphate (5-APAS-CTP) contains an aryl azide group approximately 10 A from the nucleotide base and specifically replaced CTP during synthesis of **RNA** by both **polymerases**. **Analog** was placed at the 3' end or internally within **RNA**. Both **polymerases** inefficiently incorporated two 5-APAS-CMP molecules sequentially, as was found for the related 5-APAS-UMP. **Analog** was placed at the 3' end of **RNA** in transcription complexes paused at the site of Q-modification of E. coli **RNA polymerase**, downstream of the lambda PR' promoter (+16), a pause that requires specific DNA sequences but no apparent **RNA** hairpin. Crosslinking was examined in the presence and absence of the NusA protein, which enhances the transcriptional pause at this site and is required for Q modification of the **polymerase**. Crosslinking of the 3' end of the **RNA** to NusA was not observed, consistent with our earlier results involving a NusA-enhanced pause site downstream from an **RNA** hairpin.

10/3,AB/43 (Item 43 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08029271 93312541 PMID: 7763730
Cloning, expression, and characterization of a synthetic **analog** to the bioadhesive precursor protein of the sea mussel Mytilus edulis.
Salerno AJ; Goldberg I
Biotechnology Department, Allied Signal Inc., Morristown, NJ 07962.
Applied microbiology and biotechnology (GERMANY) May **1993**, 39 (2) p221-6, ISSN 0175-7598 Journal Code: AMC
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Repetitious gene cassettes that encode the consensus decapeptide repeat of Mytilus edulis bioadhesive protein were designed, constructed, and expressed in Escherichia coli. The bioadhesive precursor (BP) with a relative molecular mass of 25,000 was expressed from one 600-bp gene at levels approaching 60% of total cell protein in strains employing T7 **RNA polymerase** for induction and carrying a repetitious gene comprised of a 30-bp unit repeat that accounts for E. coli codon bias. BP forms intracellular inclusions and yet methionine was processed from the N-terminus of the purified protein, as shown by amino acid composition and N-terminal sequencing, to give an authentic consensus precursor protein.

10/3,AB/44 (Item 44 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07968031 94072578 PMID: 8251501
Mapping the central fold of tRNA2(fMet) in the P site of the Escherichia coli ribosome.
Rosen KV; Alexander RW; Wower J; Zimmermann RA
Department of Biochemistry and Molecular Biology, University of Massachusetts, Amherst 01003.
Biochemistry (UNITED STATES) Nov 30 **1993**, 32 (47) p12802-11, ISSN 0006-2960 Journal Code: A0G
Contract/Grant No.: GM22807, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
4-Thiouridine (s4U), a photoreactive **analog** of uridine, was randomly incorporated into tRNA2(fMet) precursor molecules by transcription with T7 **RNA polymerase** . The s4U-containing transcripts were trimmed at their 5'-ends with RNase P **RNA** to yield mature tRNA2(fMet). The photoreactive tRNA2(fMet) derivatives were aminoacylated and bound to the P site of 70S ribosomes from Escherichia coli in the presence of a poly(A,G,U) template. Irradiation of the complexes at 300 nm resulted in the covalent cross-linking of tRNA2(fMet) to ribosomal proteins and rRNAs within both the 50S and 30S subunits. The labeled proteins were identified as L1, L27, and S19. 50S-subunit proteins L1 and L27 were attached to nucleotide U17 or U17.1 within the D loop of tRNA2(fMet), whereas 30S-subunit protein S19 was cross-linked to nucleotide U47 in the variable loop. Both of these sites occur in or near the central fold of the tRNA. These results permit us to map the D loop of P site-bound tRNA to the region between the central protuberance and the L1 ridge on the 50S ribosomal subunit, while the variable loop can be placed above the cleft on the head of the 30S subunit.

10/3,AB/45 (Item 45 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07855364 93186815 PMID: 8444880
The TyrR protein of Escherichia coli, analysis by limited proteolysis of

domain structure and ligand-mediated conformational changes.
Cui J; Somerville RL
Department of Biochemistry, Purdue University, West Lafayette, Indiana 47907-1153.
Journal of biological chemistry (UNITED STATES) Mar 5 **1993**, 268 (7) p5040-7, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM22131, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The TyrR protein of Escherichia coli K12 is a homodimer containing 513 amino acids/subunit. This protein is important in the transcriptional regulation of several genes whose protein products catalyze steps in aromatic amino acid biosynthesis or transport. Methods were developed for efficiently purifying the TyrR protein to apparent homogeneity. We analyzed the pattern of cleavage of the TyrR protein by trypsin, either in the absence of ligands or in the presence of saturating levels of L-tyrosine, ATP, or poly(dI-dC). At low (1:200 ratio by weight) trypsin levels, in the absence of ligands, two major digestion products accumulated. These were polypeptides of 22 and 31 kDa, shown to contain amino acid residues 1-190 and 191-467, respectively. The pattern of trypsin cleavage was unaffected by tyrosine. In the presence of ATP, an intermediate species of 53 kDa, probably containing amino acid residues 1-467, was observed. The kinetics of appearance of the 53-kDa species were consistent with a role for ATP in accelerating the hydrolysis of the R467-F468 peptide bond. The 53-kDa polypeptide underwent further tryptic hydrolysis to yield fragments of 22 and 31 kDa. When both tyrosine and ATP were present, the rate of formation of the 22- and 31-kDa fragments was more rapid than in the absence of these ligands. It appears that when both ligands are bound, the rates of hydrolysis of peptide bonds R190-Q191 and R467-F468 are both enhanced. Additional limited proteolysis experiments suggested that polypeptide segment 191-467 contains ATP binding site(s), and that the rate of cleavage of peptide bonds R190-Q191 and R467-F468 is altered when the TyrR protein interacts with poly(dI-dC), an **analog** of target DNA. Our results reveal the presence of two major structural domains within the TyrR protein. The first domain (amino acid residues 1-190) is extremely resistant to hydrolysis by trypsin. The second domain (residues 191-467), which is likely to contain ATP-binding site(s), is homologous to several other transcriptional activators specific for promoters responsive to the sigma 54 form of **RNA polymerase**. The remainder of the TyrR protein (residues 468-513) contains the operator recognition elements, probably arranged in the form of a helix-turn-helix motif. This polypeptide segment was not detected as a discrete tryptic hydrolysis product.

10/3,AB/46 (Item 46 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07833390 91294165 PMID: 1906060
Expression of ClpB, an **analog** of the ATP-dependent protease regulatory subunit in Escherichia coli, is controlled by a heat shock sigma factor (sigma 32).
Kitagawa M; Wada C; Yoshioka S; Yura T
Institute for Virus Research, Kyoto University, Japan.
Journal of bacteriology (UNITED STATES) Jul **1991**, 173 (14) p4247-53, ISSN 0021-9193 Journal Code: HH3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Escherichia coli K-12 produces at least two ATP-dependent proteases, Lon (La) and Clp (Ti), the latter consisting of a regulatory subunit (ClpA) and a proteolytic subunit (ClpP). The gene clpB encoding an **analog** of ClpA had been found at 57 min on the E. coli chromosome. Cloning and examination of novel heat shock promoters led us to identify a major clpB

promoter specifically controlled by a heat shock sigma factor, sigma 32 (the rpoH [= htpR] gene product). beta-Galactosidase synthesis from a PclpB-lacZ operon fusion was transiently induced upon temperature shift from 30 to 42 degrees C, and the induction depended on the rpoH function. Chromosomal clpB transcripts also increased upon temperature upshift and were totally absent in the rpoH deletion strain. In the in vitro transcription experiments, the clpB promoter was specifically recognized and transcribed by **RNA polymerase** -sigma 32. Nucleotide sequencing and determination of mRNA start sites permitted us to identify a major heat shock promoter located upstream of the clpB coding sequence. The results clearly indicate that clpB expression is under direct control of sigma 32. Since ClpP was recently shown to be a sigma 32-dependent heat shock protein, the present finding suggests the possibility that a potential ATP-dependent protease, ClpB-ClpP complex, plays an important role against thermal stress in E. coli.

10/3,AB/47 (Item 47 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07810229 93033116 PMID: 1413505
Transcription dependence of DNA packaging of bacteriophages T3 and T7.
Hashimoto C; Fujisawa H
Department of Botany, Faculty of Science, Kyoto University, Japan.
Virology (UNITED STATES) Nov **1992**, 191 (1) p246-50, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
T3 and T7 phages package homologous DNA more efficiently than heterologous DNA and recombinant plasmids carrying DNA sequences necessary for DNA packaging (pac sequence). The pac sequence contains a promoter for phage **RNA polymerase** and transcription from the promoter is necessary for DNA packaging. T3 and T7 **RNA polymerases** are stringently specific for their own promoters. To examine the relationship between DNA packaging and transcription, we constructed a cleared in vitro system for packaging T3 or T7 DNA containing an ammonium sulfate fractionate of a high-speed supernatant of phage-infected cells. In the system, DNA packaging required GTP and was inhibited by the 3'-deoxy **analog** of GTP, ATP, or CTP. The DNA packaging activity paralleled the transcriptional activity, assayed by incorporation of [32P]UTP into acid-insoluble material. In the system, homologous DNA was packaged more efficiently than heterologous DNA, but heterologous DNA was packaged as efficiently as homologous DNA by the addition of heterologous phage **RNA polymerase** , demonstrating that the transcriptional specificity determines the DNA packaging specificity of T3 and T7.

10/3,AB/48 (Item 48 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07808057 92408009 PMID: 1527853
Internal entry of ribosomes on a tricistronic mRNA encoded by infectious bronchitis virus.
Liu DX; Inglis SC
Department of Pathology, University of Cambridge, United Kingdom.
Journal of virology (UNITED STATES) Oct **1992**, 66 (10) p6143-54 , ISSN 0022-538X Journal Code: KCV
Erratum in J Virol 1992 Nov;66(11) 6840
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
mRNA3 specified by the coronavirus infectious bronchitis virus appears to be functionally tricistronic, having the capacity to encode three small

proteins (3a, 3b, and 3c) from separate open reading frames (ORFs). The mechanism by which this can occur was investigated through in vitro translation studies using synthetic mRNAs containing the 3a, 3b, and 3c ORFs, and the results suggest that translation of the most distal of the three ORFs, that for 3c, is mediated by an unconventional, cap-independent mechanism involving internal initiation. This conclusion is based on several observations. A synthetic mRNA whose peculiar 5' end structure prevents translation of the 5'-proximal ORFs (3a and 3b) directs the synthesis of 3c normally. Translation of 3c, unlike that of 3a and 3b, was insensitive to the presence of the 5' cap **analog** 7-methyl-GTP, and it was unaffected by alteration of the sequence contexts for initiation on the 3a and 3b ORFs. Finally, an mRNA in which the 3a/b/c infectious bronchitis virus coding region was placed downstream of the influenza A virus nucleocapsid protein gene directed the efficient synthesis of 3c as well as nucleocapsid protein, whereas initiation at 3a and 3b could not be detected. Expression of the 3c ORF from this mRNA, however, was abolished when the 3a and 3b coding region was deleted, indicating that 3c initiation is dependent on upstream sequence elements which together may serve as a ribosomal internal entry site similar to those described for picornaviruses.

10/3,AB/49 (Item 49 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07804581 92338156 PMID: 1321660
Proximity between nucleotide/dinucleotide and metal ion binding sites in DNA-dependent **RNA polymerase** from Escherichia coli.
Tyagi SC; Wu FY
Department of Biochemistry and Cell Biology, State University of New York, Stony Brook 11794-5215.
Biochemistry (UNITED STATES) Jul 21 **1992**, 31 (28) p6447-53, ISSN 0006-2960 Journal Code: A0G
Contract/Grant No.: GM28057, GM, NIGMS; HL14262, HL, NHLBI
Erratum in Biochemistry 1994 Aug 2;33(30) 9032
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In order to understand translocation in transcription, it is important to develop a continuous functional assay for **RNA polymerase** (RNAP) activity in vitro. Fluorescent derivatives of ATP, UTP, UpA, and CpA with aminonaphthalene-5-sulfonic acid (AmNS) attached to the nucleotide triphosphates via a gamma-phosphoramidate bond or to the dinucleotide monophosphates via a 5'-secondary amine linkage were synthesized [Tyagi, S.C., & Wu, F.Y.-H. (1987) J. Biol. Chem. 262, 10684-10688]. The fluorescent emission spectra of (5'-AmNS)UpA, (5'-AmNS)CpA, (gamma-AmNS)ATP, and (gamma-AmNS)UTP overlap the absorption spectrum of co-substituted **RNA polymerase** (Co-RNAP) and ensure fluorescence resonance energy transfer (FRET) between the fluorescent **analog** and Co(II) in Co-RNAP. The binding constants at a single site for (gamma-AmNS)ATP, (gamma-AmNS)UTP, (5'-AmNS)UpA, and (5'-AmNS)CpA were observed to be 7.11, 5.26, 0.52, and 0.61 microM, respectively, in Co-RNAP and 5.70, 3.42, 0.12, and 0.21 microM, respectively, in Zn-RNAP. (8-AmTEMPO)ATP, with the spin probe AmTEMPO attached to the C-8 position at ATP [Tyagi, S.C. (1991) J. Biol. Chem. 266, 17936-17940], and Mn(3'-OCH3)UTP were synthesized. Mn-(II)-substituted **RNA polymerase** (Mn-RNAP) is prepared. The single site binding constants for (8-Am-TEMPO)ATP and Mn(3'-OCH3)UTP were 3.58 and 2.35 microM in Zn-RNAP and 5.77 and 3.43 microM in Mn-RNAP, respectively. These results indicate that dinucleotides bind much more tightly than mononucleotides to RNAP and that the binding constants are roughly the same for both Co- and Zn-substituted RNAP.(ABSTRACT TRUNCATED AT 250 WORDS)

10/3,AB/50 (Item 50 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07804093 92329494 PMID: 1627602
Mapping of the active site of T7 **RNA polymerase** with 8-azidoATP.
Knoll DA; Woody RW; Woody AY
Department of Biochemistry, Colorado State University, Fort Collins 80523.
Biochimica et biophysica acta (NETHERLANDS) Jun 24 **1992**, 1121 (3) p252-60, ISSN 0006-3002 Journal Code: A0W
Contract/Grant No.: GM-23697, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The photoaffinity **analog** of ATP, 8-azidoATP, labels T7 **RNA polymerase** . Photoincorporation exhibits saturation behavior and is protected against by the substrate ATP. 8-AzidoATP is a competitive inhibitor of ATP incorporation with Ki approximately 40 microM. The photolabeled T7 **RNA polymerase** , following cyanogen bromide digestion, was analyzed by phenylboronate agarose column chromatography followed by reverse-phase high pressure liquid chromatography. Sequencing of the peptides labeled with radioactive photoprobe allowed the identification of three peptides, P314-M362 (I), L550-M666 (II), and F751-M861 (III). These peptides are in the proximity of the photoprobe 8-azidoATP and, therefore, expected to contain functionally significant residues and define an active site domain. These peptides (I and II) contain residues previously implicated in T7 **RNA polymerase** activity or show homology to active site regions of the Klenow fragment of DNA **polymerase** I (II and III).

10/3,AB/51 (Item 51 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07803587 92319642 PMID: 1620609
Joints formed by RecA protein from oligonucleotides and duplex DNA block initiation and elongation of transcription.
Golub EI; Ward DC; Radding CM
Department of Genetics, Yale University School of Medicine, New Haven, CT 06510.
Nucleic acids research (ENGLAND) Jun 25 **1992**, 20 (12) p3121-5, ISSN 0305-1048 Journal Code: O8L
Contract/Grant No.: GM 40633, GM, NIGMS; HG 00338, HG, NHGRI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In the presence of the non-hydrolyzable **analog** of ATP, ATP gamma S, RecA protein can polymerize on an oligodeoxy-ribonucleotide to form a stable oligonucleoprotein filament that can find its homologous sequence in double-stranded DNA. The homologous joint formed by the oligonucleotide and duplex DNA is stable only if RecA protein is not removed. Such a nucleoprotein joint, covering a part or all of the promoter region of T3 or T7 phage **RNA polymerase** , blocked transcription directed by those **polymerases**. The same kind of joint, located downstream of the **RNA polymerase** promoter, also inhibited elongation of transcription and caused accumulation of truncated transcripts. These observations suggest that RecA protein can be used to shut off transcription from any promoter of known sequence.

10/3,AB/52 (Item 52 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07786388 92109706 PMID: 1764057
Gene expression from multicopy T7 promoter vectors proceeds at single copy rates in the absence of T7 **RNA polymerase**.
Somerville RL; Shieh TL; Hagewood B; Cui JS
Department of Biochemistry, Purdue University West Lafayette, IN 47907.
Biochemical and biophysical research communications (UNITED STATES) Dec 31 **1991**, 181 (3) p1056-62, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Three different genes (trpR+, tyrR+ and phi (trpR-lacZ)) were inserted into pET3a, a multicopy transcription-translation vector designed by Rosenberg et al. (1) for the T7 **RNA polymerase** -driven overexpression of proteins in Escherichia coli. Gene orientation was in the anticlockwise ("silent") direction. Gene expression in the absence of T7 **RNA polymerase** was evaluated either directly using lacZ reporter systems or indirectly by observing the susceptibility of plasmid-bearing tester strains to inhibition by an aromatic amino acid **analog** . The production of repressor proteins and of a Trp repressor-LacZ chimera was readily detected, at levels comparable to those of haploid trpR+ or tyrR+ E. coli strains. Such T7 vector constructs thus have two especially useful properties: first, they provide a means for the high-level production of various proteins in E. coli; second, they offer a technically advantageous point of departure for structure-function studies of genes whose overexpression from multicopy plasmids would normally be cytotoxic.

10/3,AB/53 (Item 53 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07777166 91311670 PMID: 1713273
Sigma subunit of Escherichia coli **RNA polymerase** loses contacts with the 3' end of the nascent **RNA** after synthesis of a tetranucleotide.
Bowser CA; Hanna MM
Department of Biological Chemistry, University of California, Irvine 92717.
Journal of molecular biology (ENGLAND) Jul 20 **1991**, 220 (2) p227-39, ISSN 0022-2836 Journal Code: J6V
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have used photocrosslinking to analyze the contacts between the 3' end of the **RNA** and Escherichia coli **RNA polymerase** during the early steps of **RNA** synthesis using the nucleotide **analog** 8-azido-ATP (8-N3-ATP). The crosslinking group on 8-N3-ATP contacts the beta, beta' and sigma subunits when the **analog** is bound to the holoenzyme. We show here that 8-N3-ATP is a substrate for E. coli **RNA polymerase** and acts as an **RNA** chain terminator when incorporated into the 3' end of nascent **RNA** . 8-N3-AMP was incorporated uniquely at the 3' end of tri-, tetra- and pentanucleotides synthesized from a poly[d(A-T)] template and at the 3' end of pentanucleotides from two promoters (lambda PR' and E. coli rrnB P1). The oligonucleotides were covalently attached to the **RNA polymerase** by irradiation of transcription complexes with ultraviolet light. All RNAs labeled the beta and beta' subunits, but sigma was contacted only by the trinucleotide and tetranucleotide on poly[d(A-T)]. Sigma is still present in transcription complexes containing the pentanucleotide on poly[d(A-T)], despite the lack of labeling. Neither pentanucleotide from the authentic promoters contacted sigma. We conclude that as holoenzyme moves downstream, either two separate conformational changes occur, after synthesis of the trinucleotide and tetranucleotide, which result in movement of sigma away from the nucleotide binding site or, alternatively, sigma remains fixed

relative to the DNA while the domain on core **polymerase** forming the nucleotide binding site moves downstream.

10/3,AB/54 (Item 54 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07776661 91302362 PMID: 1712778
Discrete functional stages of vaccinia virus early transcription during a single round of **RNA** synthesis in vitro.
Luo Y; Hagler J; Shuman S
Program in Molecular Biology, Sloan-Kettering Institute, New York, New York 10021.
Journal of biological chemistry (UNITED STATES) Jul 15 **1991**, 266 (20) p13303-10, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM 42498-02, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have developed a system for analysis of discrete steps in vaccinia virus early mRNA synthesis during a single round of transcription in vitro. A synthetic early promoter is used to direct transcription by vaccinia **RNA polymerase** of a G-less cassette in linear duplex DNA. Omission of GTP from transcription reactions leads to the formation of ternary elongation complexes paused stably at the end of the G-less cassette. These complexes can be induced to elongate by provision of GTP. While initiation of transcription is sensitive to low concentrations of salt and Sarkosyl, elongation is relatively resistant to these agents. Termination can be studied in a single synthetic cycle by forming transcription complexes paused just proximal to the termination signal TTTTTNT that can subsequently elongate and terminate. By selectively incorporating the termination-inhibiting **analog** BrUMP into proximal and distal portions of the nascent transcript, we localize the termination signal within or near the sequence UUUUUNU in the nascent **RNA**. We show that access of the vaccinia termination factor (VTF/capping enzyme) to the transcriptional apparatus can occur subsequent to initiation and synthesis of a 390-nucleotide nascent **RNA** . Termination is more sensitive to inhibition by salt and Sarkosyl than in elongation. This sensitivity is not reversed by preincubation of VTF with the transcription complex. Finally, we confirm the identity of VTF and vaccinia mRNA capping enzyme by demonstration of VTF activity associated with capping enzyme expressed in Escherichia coli.

10/3,AB/55 (Item 55 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07774181 91251261 PMID: 1645806
Photoaffinity labeling of rotavirus VP1 with 8-azido-ATP: identification of the viral **RNA polymerase**.
Valenzuela S; Pizarro J; Sandino AM; Vasquez M; Fernandez J; Hernandez O; Patton J; Spencer E
Unidad de Virologia, INTA, Universidad de Chile, Santiago.
Journal of virology (UNITED STATES) Jul **1991**, 65 (7) p3964-7, ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: AI00990, AI, NIAID; AI21478, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Rotavirus single-shelled particles have several enzymatic activities that are involved with the synthesis of capped mRNAs both in vivo and in vitro. Because single-shelled particles must be structurally intact to carry out transcription, it has proven to be difficult to identify the protein within such particles that possesses associated **RNA polymerase**

activity. One approach for characterizing the function of the individual proteins within single-shelled particles is to use nucleotide **analogs** to specifically label those proteins, such as the viral **RNA polymerase**, that have affinity for nucleotides. In this study, 8-azido-ATP (azido-ATP), a photoreactable nucleotide **analog**, was used to identify the viral **RNA polymerase** on the basis of the ability of the **analog** to inhibit transcription activity associated with rotavirus particles on exposure to UV light. When single-shelled particles were treated with UV light in the presence of [alpha-32P]azido-ATP, the structural protein VP1 became radiolabeled because of cross-linking of the nucleotide **analog**, and there was a corresponding decrease in the ability of the particles to synthesize mRNA. In parallel experiments in which single-shelled particles were not exposed to UV light, VP1 was not radiolabeled and the particles successfully used azido-ATP as a substrate for the synthesis of viral mRNAs. Taken together, these results are consistent only with the conclusion that VP1 is the rotavirus **RNA**-dependent **RNA polymerase**.

10/3,AB/56 (Item 56 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07693379 93162870 PMID: 1286940
Structure-toxicity relationships in the amatoxin series. Structural variations of side chain 3 and inhibition of **RNA polymerase** II.
Zanotti G; Petersen G; Wieland T
Department of Pharmaceutical Sciences, University La Sapienza, Rome, Italy.
International journal of peptide and protein research (DENMARK) Dec **1992**, 40 (6) p551-8, ISSN 0367-8377 Journal Code: GSD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The amatoxins, highly toxic components of death cap Amanita mushrooms, bind strongly to **RNA polymerase** II (or B) in cell nuclei thus preventing the transcription of DNAs to hn-RNAs (Pre-mRNAs), the precursors of messenger RNAs. Three of the binding sites of the bicyclic octapeptides have been identified: an isoleucine side chain in position 6, a trans-4-hydroxyl group at proline in position 2 and a hydroxylated L-isoleucine side chain in position 3. No information exists about the stereochemical conditions at the beta-C-atom (C-atom 3) of this side chain. We have now synthesized the diastereomeric S-deoxo-amaninamides (Fig. 1) containing, in position 3, L-allo-isoleucine (**analog** 1), (2S, 3R)-2-amino-4-hydroxy-3-methyl butyric acid (**analog** 2), the diastereomer (2S, 3S)-2-amino-4-hydroxy-3-methylbutyric acid (**analog** 3) and D-isoleucine (**analog** 4). In the last synthesis, besides the "normal" bicyclic octapeptide 4, an isomeric Iso-4 was formed. The affinities for Drosophila **RNA polymerase** II were 100 times weaker as compared to gamma-amanitin for 1, 10 times weaker for 2, 200 times weaker for 3, 100 times weaker for 4, and more than 1000 times weaker for Iso-4. The results point to the importance of a methyl group in (R)-configuration at the beta-C atom of side chain 3.

10/3,AB/57 (Item 57 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07422980 91332088 PMID: 1869572
A role for ATP hydrolysis in vaccinia virus early gene transcription. Dissociation of the early transcription factor-promoter complex.
Broyles SS
Department of Biochemistry, Purdue University, West Lafayette, Indiana 47907.
Journal of biological chemistry (UNITED STATES) Aug 15 **1991**, 266

(23) p15545-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: AI28432-02, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Vaccinia virus **RNA polymerase** requires the vaccinia early transcription factor, VETF, for the in vitro initiation of transcription at early gene promoters in a reaction requiring ATP hydrolysis. VETF binds specifically to early gene promoters and has an associated DNA-dependent ATPase activity. The effect of ATP on the interaction of VETF with the promoter for the vaccinia growth factor gene promoter has been examined. ATP had no marked effect on the steady-state level of promoter binding but dramatically affected the kinetics of dissociation of VETF from the promoter. The half-life of the VETF-promoter complex was greatly reduced in the presence of ATP. The destabilization of the complex was specific for ATP and dATP, consistent with the substrate specificity of the VETF-associated ATPase. ADP or the non-hydrolyzable ATP **analog** adenylyl-imidodiphosphate did not destabilize the complex suggesting that ATP hydrolysis is obligatory for dissociation. These findings provide a link between the promoter binding and ATPase activities associated with VETF and suggest that the ATP-dependent dissociation of the VETF-promoter complex is an important event in the transcription of vaccinia virus early genes.

10/3,AB/58 (Item 58 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07350720 90297623 PMID: 2141779
Age-related differences in pharmacokinetics of phosphonoformate in cats.
Swenson CL; Sams RA; Polas PJ; Michael DF; Mathes LE
Department of Veterinary Pathobiology, Ohio State University, Columbus 43210.
Antimicrobial agents and chemotherapy (UNITED STATES) May **1990**, 34 (5) p871-4, ISSN 0066-4804 Journal Code: 6HK
Contract/Grant No.: NO1-AI-62525, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Phosphonoformate (PFA) is a simple PPi **analog** which inhibits the activities of a variety of viral DNA **polymerase**, **RNA polymerase** , and reverse transcriptase enzymes. PFA is a topical and parenteral treatment for human herpesvirus infections and is currently in phase I trials for treatment of acquired immunodeficiency syndrome. Pharmacokinetic properties of PFA in young (growing) and adult specific-pathogen-free cats were compared. Mean PFA clearance from plasma was twofold higher in young cats (7.52 ml/min per kg of body weight) than in adult cats (3.70 ml/min per kg). Higher PFA clearance from plasma observed in young cats may result from higher renal clearance or enhanced accumulation of PFA in bone tissue of young versus adult cats. No plasma protein binding of PFA was observed. Mean oral bioavailability was 35% in young cats. These data indicate that age-related differences in PFA clearance from plasma occur in cats.

10/3,AB/59 (Item 59 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07227646 90320144 PMID: 2371774
Infectious in vitro transcripts from a plum pox potyvirus cDNA clone.
Riechmann JL; Lain S; Garcia JA
Centro de Biologia Molecular, CSIC-UAM, Universidad Autonoma de Madrid, Spain.
Virology (UNITED STATES) Aug **1990**, 177 (2) p710-6, ISSN

0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A full-length cDNA clone of the 9786 nt plum pox virus (PPV) **RNA** genome has been cloned downstream from a phage T7 **RNA** **polymerase** promoter. The RNAs synthesized by in vitro run-off transcription in the presence of the 5' cap **analog** m7GpppG were infectious in Nicotiana clevelandii plants. No infectivity was detected when the transcriptions were carried out in the absence of the cap **analog** . Inoculations of the local lesion host Chenopodium foetidum indicated that the infectivity of the synthetic transcripts was about 1% of that of the native viral **RNA**. An extra G present at the 5' terminus of the transcripts was lost during their replication in plants, and the typical length distribution of the poly(A) tails was recovered. The viral **RNA** recovered from transcript-infected plants had approximately the same specific infectivity as native viral **RNA** . A G/A sequence heterogeneity found between different cDNA subgenomic clones was used to demonstrate that the infections were caused by the in vitro transcripts and were not the result of contamination.

10/3,AB/60 (Item 60 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07142865 93366790 PMID: 7689559
Mechanism of DmS-II-mediated pause suppression by Drosophila **RNA** **polymerase** II.
Guo H; Price DH
Department of Biochemistry, University of Iowa, Iowa City 52242.
Journal of biological chemistry (UNITED STATES) Sep 5 **1993**, 268 (25) p18762-70, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Transcription elongation factor S-II mediates nascent transcript cleavage by **RNA** **polymerase** II (Reines, D. (1992) J. Biol. Chem. 267, 3795-3800). We have examined the mechanism of action of the Drosophila S-II **analog** , DmS-II, in a defined transcription system. Our results show that DmS-II is necessary and sufficient to activate nascent transcript cleavage by **RNA** **polymerase** II during transcription of a dC-tailed template. The pattern of transcripts resulting from prolonged action by DmS-II indicates that there are kinetic barriers to transcript shortening. During the cleavage reaction, the **polymerase** remains in register with the template strand and generates mainly nucleotide dimers. The ability of DmS-II to mediate transcript shortening resides in the carboxyl-terminal half of the protein. Our results support a model for pause suppression in which DmS-II binds to the paused **polymerase**, causes one cleavage event and is then released from the complex. Elongation by the **polymerase** then allows a second encounter with the pause site and a second chance of passing the site. Complete pause suppression may require multiple transcript shortening events for some **polymerase** molecules.

10/3,AB/61 (Item 61 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07036474 93165722 PMID: 8434011
Characterization of a host protein associated with brome mosaic virus **RNA**-dependent **RNA** **polymerase**.
Quadt R; Kao CC; Browning KS; Hershberger RP; Ahlquist P
Institute for Molecular Virology, University of Wisconsin-Madison 53706.
Proceedings of the National Academy of Sciences of the United States of

America (UNITED STATES) Feb 15 **1993**, 90 (4) p1498-502, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: CA09075, CA, NCI; GM35072, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The association of host proteins with viral **RNA** replication proteins has been reported for a number of (+)-strand **RNA** viruses. However, little is known about the identity or function of these host proteins in viral replication. In this paper we report the characterization of a host protein associated with the **RNA**-dependent **RNA polymerase** (RdRp) from brome mosaic virus (BMV)-infected barley. A host protein was specifically and proportionally enriched with BMV RdRp activity through several purification steps. This RdRp-associated host protein reacted with an antiserum prepared against wheat germ eukaryotic translation initiation factor 3 (eIF-3). The RdRp-associated host protein, the p41 subunit of wheat germ eIF-3, and an antigenically related protein from rabbit reticulocyte lysates were all found to bind with high affinity and specificity to BMV-encoded protein 2a, which is involved in viral **RNA** replication. Moreover, addition of wheat germ eIF-3 or the p41 subunit from wheat germ to BMV RdRp gave a specific and reproducible 3-fold stimulation of (-)-strand **RNA** synthesis in vivo. These results suggest that the barley **analog** of eIF-3 subunit p41, or a closely related protein, associates with BMV RdRp in vivo and is involved in BMV **RNA** replication. This observation and the established role of translation factors in bacteriophage Q beta RdRp suggest that association with translation factors may be a general feature of **RNA** replication by (+)-strand **RNA** viruses.

10/3,AB/62 (Item 62 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06987171 90384482 PMID: 2119479
Increased half-life of mu immunoglobulin mRNA during mouse B cell development increases its abundancy.
Genovese C; Milcarek C
Department of Microbiology, Biochemistry and Molecular Biology, University of Pittsburgh School of Medicine, PA 15261.
Molecular immunology (ENGLAND) Aug **1990**, 27 (8) p733-43, ISSN 0161-5890 Journal Code: NG1
Contract/Grant No.: CA 36606, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

When B cells encounter antigen, the cells mature into terminally differentiated plasma cells and the amount of steady-state immunoglobulin (Ig) mu mRNA is increased 23-60-fold over the amount seen in earlier B cell stages. Most of this dramatic increase in Ig gene mRNA accumulation could be due to post-transcriptional regulation. We have treated a series of mouse cell lines fixed at different stages of B cell differentiation with an adenosine nucleotide **analog** 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole (DRB) which specifically blocks synthesis of new **RNA polymerase** II transcripts. The amount of mu heavy chain cytoplasmic **RNA**, measured by quantitative Northern blot analysis at various times post DRB treatment, is reflective of the transcript's stability. The mu mRNA half-life values observed from the earliest-stage lymphomas (70Z/3 and WEHI-231) are about 1.9-4 hr, whereas the t1/2 of mu mRNA in the hybridomas (Hyb54.3C2 and IdG11) is about 13-17 hr. There is, therefore, a nine-fold maximal increase in half-life of the mu mRNA in the Hyb54.3C2 over that observed in the earliest stage (70Z/3) cells.

10/3,AB/63 (Item 63 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

06959837 90336647 PMID: 1696203
Inactivation of bacteriophage T7 DNA-dependent **RNA polymerase** by 5'-p-fluorosulfonylbenzoyladenosine. Identification of the modification site and the effect of the modification on enzyme action.
Tunitskaya VL; Akbarov AKh; Luchin SV; Memelova LV; Rechinsky VO; Kochetkov SN
V. A. Engelhardt Institute of Molecular Biology, USSR Academy of Sciences, Moscow.
European journal of biochemistry (GERMANY, WEST) Jul 20 **1990**, 191 (1) p99-103, ISSN 0014-2956 Journal Code: EMZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Bacteriophage T7 **RNA polymerase** was covalently modified by 5'-[4-fluorosulfonyl)benzoyl]adenosine (4-FSO2BzAdo). The modified enzyme lacks the ability to catalyze **RNA** synthesis from the phi 10 promoter of bacteriophage T7; both promoter and GTP binding being markedly decreased. The mild hydrolysis of the ester bond of 4-FSO2BzAdo within the covalent enzyme-inhibitor complex restores the **RNA** synthesis at a lower rate. Sequence studies show that Lys172 is the target of modification by 4-FSO2BzAdo. This residue, which is situated in the polypeptide region connecting two domains of **RNA polymerase**, was shown to be the primary site of the limited proteolysis occurring in vivo [Ikeda, R. A. & Richardson, C. C. (1987) J. Biol. Chem. 262, 3790-3799]. We propose that Lys172 is located outside the active site. Once this residue has reacted with 4-FSO2BzAdo, the nucleoside moiety of the **analog** is fixed in the NTP-binding site of the active centre and prevents binding of the substrates. Here, Lys172 per se is not important for the activity but serves as an 'anchor' for binding of the inhibitor.

10/3,AB/64 (Item 64 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06955141 90237075 PMID: 1692025
Active site labeling of Escherichia coli transcription elongation complexes with 5-[4-azidophenacyl)thio)uridine 5'-triphosphate.
Dissinger S; Hanna MM
Department of Biological Chemistry, California College of Medicine, University of California, Irvine 92717.
Journal of biological chemistry (UNITED STATES) May 5 **1990**, 265 (13) p7662-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM07134-14, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Escherichia coli **RNA polymerase** transcription elongation complexes have been prepared that contain a photo-cross-linking uridine **analog** at only the 3' end, or one or two nucleotides removed from the 3' end, in the nascent **RNA** chain. Additionally, complexes have been isolated in which the **analog** has been substituted for every UMP residue, at positions ranging from 20 to 140 nucleotides from the 3' end. The **RNA** has been photochemically cross-linked to the **RNA polymerase** to identify the subunits that form the binding site(s) for these regions in the nascent **RNA**. The photo-cross-linking nucleotide **analog** used for these studies was 5-[4-azidophenacyl)thio)uridine-5'-triphosphate (5-APAS-UTP), which acts as a 10-15 A probe. With 5-APAS-UMP positioned only at the 3' end of the **RNA**, or one or two nucleotides from the 3' end, only the beta subunit appeared to be contacted. When the **analog** was positioned throughout the **RNA**, both the beta and beta' subunits were contacted. No labeling of the sigma or alpha subunits was observed with any **RNA** length. In addition to placing this

analog at specific positions in short RNAs, we have carried out transcription studies with 5-APAS-UTP to determine the optimal UTP to **analog** ratio for production of full length, photoreactive transcripts. Surprisingly, we found that when transcription complexes were stalled shortly after initiation, by deletion of one ribonucleoside triphosphate to synchronize transcription, changes in transcriptional pausing occurred downstream. These results suggest that events that occur early in transcription can affect the elongation and/or termination events that occur far downstream from the promoter. This effect occurred even with UTP but was greatly enhanced by replacement of UTP with either this **analog** or 4-thio-UTP. By enhancing the normal transcriptional pausing event, these **analogs** can serve as probes of the conformational changes that may exist in paused transcription complexes.

10/3,AB/65 (Item 65 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06951980 90154051 PMID: 2303478
Photoaffinity labeling of **RNA polymerase** III transcription complexes by nascent **RNA**.
Bartholomew B; Meares CF; Dahmus ME
Department of Chemistry, University of California, Davis 95616.
Journal of biological chemistry (UNITED STATES) Mar 5 **1990**, 265 (7) p3731-7, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM 25909, GM, NIGMS; GM 33300, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The proteins contacting nascent **RNA** transcripts in **RNA polymerase** III transcription complexes have been examined using photoaffinity labeling techniques. The photoaffinity **analog** 4-S-UTP was incorporated along with [alpha-32P]CTP into VAI transcripts, using a phosphocellulose fractionated HeLa S-100 extract and DNA containing the adenovirus VAI gene. The photoreactive nascent **RNA** was cross-linked to proximal proteins in the transcription complex. The photoaffinity labeled proteins were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and detected by autoradiography. The specific photoaffinity labeling of **RNA polymerase** III was dependent on 4-S-UTP and on DNA containing a class III promoter. Photoaffinity labeling was inhibited by 200 micrograms/ml alpha-amanitin. Proteins of 140, 160, 270, and 310 kDa were labeled. These photoaffinity labeled proteins were shown to be stably associated with the DNA template by gel exclusion chromatography. The 160-kDa protein was cross-linked to RNAs approximately 14-18 nucleotides in length, whereas the greater than 250-kDa proteins were cross-linked to RNAs 18-30 nucleotides in length. The 140- and 160-kDa proteins correspond in molecular mass to the two large subunits of **RNA polymerase** III. The molecular masses of the 270- and 310-kDa proteins, and the length of the **RNA** cross-linked to them, suggest that these proteins are components of transcription factor (TF) IIIC. These results indicate that the nascent transcript contacts the two largest subunits of **RNA polymerase** III until the transcription complex reaches the TFIIIC binding site, at which point the nascent transcript contacts TFIIIC.

10/3,AB/66 (Item 66 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06924751 92236581 PMID: 1373806
Stability of Drosophila **RNA polymerase** II elongation complexes in vitro.
Kephart DD; Marshall NF; Price DH
Department of Biochemistry, University of Iowa, Iowa City 52242.

Molecular and cellular biology (UNITED STATES) May **1992**, 12 (5)
p2067-77, ISSN 0270-7306 Journal Code: NGY
Contract/Grant No.: DK25292, DK, NIDDK; GM35500, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

We show that nuclear extract from Drosophila Kc cells supports efficient elongation by **RNA polymerase** II initiated from the actin 5C promoter. The addition of 0.3% Sarkosyl, 1 mg of heparin per ml, or 250 mM KCl immediately after initiation has two effects. First, the elongation rate is reduced 80 to 90% as a result of the inhibition of elongation factors. Second, there is an increase in the amount of long runoff **RNA**, suggesting that there is an early block to elongation that is relieved by the disruptive reagents. Consistent with the first effect, we find that the ability of factor 5 (TFIIF) to stimulate the elongation rate is inhibited by the disruptive agents when assayed in a defined system containing pure **RNA polymerase** II and a dC-tailed template. The disruptive agents also inhibit the ability of DmS-II to suppress transcriptional pausing but only slightly reduce the ability of DmS-II to increase the elongation rate twofold. The pause sites encountered by **RNA polymerase** II after initiation at a promoter and subsequent treatment with the disruptive reagents are also recognized by pure **polymerase** transcribing a dC-tailed template. It has been suggested that 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole inhibits **RNA polymerase** II during elongation, but we find that the purine nucleoside **analog** has no effect on elongation complexes containing **RNA** over 500 nucleotides in length or on the action of factor 5 or DmS-II in the defined system.

10/3,AB/67 (Item 67 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06877626 92394958 PMID: 1522107

A cap binding protein that may mediate nuclear export of **RNA polymerase** II-transcribed RNAs.

Izaurralde E; Stepinski J; Darzynkiewicz E; Mattaj IW
European Molecular Biology Laboratory (EMBL), Heidelberg, Germany.
Journal of cell biology (UNITED STATES) Sep **1992**, 118 (6)
p1287-95, ISSN 0021-9525 Journal Code: HMV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

It has previously been shown that efficient export of U1 snRNA or of microinjected, in vitro synthesized, **RNA** transcripts from the nucleus of Xenopus oocytes is facilitated by their monomethyl guanosine cap structures. Nuclear exit of these transcripts could be competitively inhibited by microinjection of an excess of a cap **analog**, the dinucleotide m7GpppG (Hamm, J., and I. W. Mattaj. 1990. Cell. 63:109-118). We have now analyzed the ability of several other related cap **analogs** to inhibit the export of U1 snRNA from the nucleus. The results define the recognition specificity of a factor(s) involved in **RNA** transport, and indicate that the cap binding activity (CBA) involved in **RNA** export is different from cap binding proteins (CBPs) involved in the initiation of translation. A CBP, whose specificity for different **analogs** correlates with the ability of the **analogs** to inhibit U1 snRNA export, is identified in nuclear extracts prepared from HeLa cells. We propose that this protein may have a role in the export of capped RNAs from the nucleus.

10/3,AB/68 (Item 68 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06865837 92375083 PMID: 1508210
Genetic interaction between transcription elongation factor TFIIS and **RNA polymerase** II.
Archambault J; Lacroute F; Ruet A; Friesen JD
Department of Genetics, Hospital for Sick Children, Toronto, Ontario, Canada.
Molecular and cellular biology (UNITED STATES) Sep **1992**, 12 (9) p4142-52, ISSN 0270-7306 Journal Code: NGY
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Little is known about the regions of **RNA polymerase** II (RNAPII) that are involved in the process of transcript elongation and interaction with elongation factors. One elongation factor, TFIIS, stimulates transcript elongation by binding to RNAPII and facilitating its passage through intrinsic pausing sites in vitro. In Saccharomyces cerevisiae, TFIIS is encoded by the PPR2 gene. Deletion of PPR2 from the yeast genome is not lethal but renders cells sensitive to the uracil **analog** 6-azauracil (6AU). Here, we show that mutations conferring 6AU sensitivity can also be isolated in the gene encoding the largest subunit of S. cerevisiae RNAPII (RPO21). A screen for mutations in RPO21 that confer 6AU sensitivity identified seven mutations that had been generated by either linker-insertion or random chemical mutagenesis. All seven mutational alterations are clustered within one region of the largest subunit that is conserved among eukaryotic RNAPII. The finding that six of the seven rpo21 mutants failed to grow at elevated temperature underscores the importance of this region for the functional and/or structural integrity of RNAPII. We found that the 6AU sensitivity of the rpo21 mutants can be suppressed by increasing the dosage of the wild-type PPR2 gene, presumably as a result of overexpression of TFIIS. These results are consistent with the proposal that in the rpo21 mutants, the formation of the RNAPII-TFIIS complex is rate limiting for the passage of the mutant enzyme through pausing sites. In addition to implicating a region of the largest subunit of RNAPII in the process of transcript elongation, our observations provide in vivo evidence that TFIIS is involved in transcription by RNAPII.

10/3,AB/69 (Item 69 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06844025 91218172 PMID: 1708833
RNA -protein interactions in a Nus A-containing Escherichia coli transcription complex paused at an **RNA** hairpin.
Dissinger S; Hanna MM
Department of Biological Chemistry, California College of Medicine, University of California, Irvine 92717.
Journal of molecular biology (ENGLAND) May 5 **1991**, 219 (1) p11-25, ISSN 0022-2836 Journal Code: J6V
Contract/Grant No.: GM07134-14, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have isolated Escherichia coli transcription complexes, paused in the presence and absence of Nus A, which contain **RNA** substituted at every UMP residue with a photocrosslinking nucleotide **analog**. The pause site is immediately downstream from an **RNA** stem-loop structure, and although pausing occurs in the absence of Nus A, it is substantially enhanced in the presence of Nus A. We have analyzed the secondary structure of this **RNA** and show that the **analog** does not interfere with the formation of the normal stem-loop structures. Additionally, the **analog** substrate does not alter transcriptional pausing, in the presence or absence of Nus A, indicating that Nus A recognition of the transcription complex is not affected by the presence of the crosslinking

groups in the **RNA**. Ribonuclease digestion of the **RNA** in paused complexes identifies two accessible regions, two nucleotides in the loop and one near the base of the upstream side of the stem-loop. Cleavage at one loop nucleotide is enhanced by Nus A, while the nucleotide near the base of the stem-loop is partially protected. Upon irradiation of the transcription complex, Nus A is not photoaffinity labeled by the **RNA**, even at a high molar ration to **RNA polymerase** (250:1). Both the beta and beta' subunits are labeled, however, indicating that the putative stem-loop binding domain on the core **polymerase** involves both subunits. Because the nucleotide protected from ribonuclease by Nus A is very near two **analogs**, yet Nus A is not crosslinked to the **RNA**, it is unlikely that Nus A could be protecting this position through direct contact. Furthermore, **analog** is substituted at positions in both the loop and at several positions in the stem, and again, no crosslinking to Nus A is observed. We conclude that enhancement of pausing by Nus A probably does not require direct interaction with the bases in the **RNA** stem-loop.

10/3,AB/70 (Item 70 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06822408 92172979 PMID: 1793747
[Mechanism of differential effect of low dose adaptogens on the functional activity of normal and transformed cellular elements in vitro]
K mekhanizmu differentsirovannogo vliianiia malykh doz adaptogenov na funktsional'nuiu aktivnost' normal'nykh i transformirovannykh kletochnykh elementov in vitro.
Udintsev SN; Shakhov VP; Borovskoi IG
Biofizika (USSR) Jul-Aug **1991**, 36 (4) p624-7, ISSN 0006-3029 Journal Code: A1S
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
Influence of water solutions of chemically pure adaptogen--synthetic **analog** of Rhodiola Rosea extract phenol composition (SAR) on functional activity of hemopoietic and tumor cells of mice with Ehrlich ascite cancer was studied in vitro. The periodical character of SAR effects was shown to be different for both types of cells, and at 1 x 10(-2) and 1 x 10(-26) M concentrations simultaneous stimulation of blood marrow cells colony-forming activity and inhibition of the latter in tumor elements was revealed. Essential changes of reactions of both cell types after adding the DNA-dependent **RNA polymerase** blocker Actinomycin D permit to suggest SAR effects to be connected with drug influence on the membrane **RNA** of the target cells.

10/3,AB/71 (Item 71 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06777276 92020839 PMID: 1924288
E1BF is an essential **RNA polymerase** I transcription factor with an intrinsic protein kinase activity that can modulate rRNA gene transcription.
Zhang J; Niu HF; Jacob ST
Department of Pharmacology and Molecular Biology, Chicago Medical School, IL 60064.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Oct 1 **1991**, 88 (19) p8293-6, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: CA31894, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

We previously described the purification and characterization of E1BF, a rat rRNA gene core promoter-binding factor that consists of two polypeptides of 89 and 79 kDa. When this factor was incubated in the absence of any exogenous protein kinase under conditions optimal for protein phosphorylation, the 79-kDa polypeptide of E1BF was selectively phosphorylated. The labeled phosphate could be removed from the E1BF polypeptide by treatment with calf intestinal alkaline phosphatase or potato acid phosphatase. Elution of the protein from the E1BF-promoter complex formed in an electrophoretic mobility-shift assay followed by incubation of the concentrated eluent with [gamma-32P] ATP resulted in the selective labeling of the 79-kDa band. The E1BF-associated protein kinase did not phosphorylate casein or histone H1. Fraction DE-B, a preparation containing **RNA polymerase** I and all **polymerase** I transcription factors (including E1BF), lost **polymerase** I transcriptional activity when treated with phosphatase. The phosphatase-induced inactivation of **polymerase** I activity associated with fraction DE-B could be reversed by the addition of purified E1BF. Treatment of purified E1BF with heat, SDS, or an ATP affinity **analog** eliminated its capacity to reactivate dephosphorylated fraction DE-B. These data demonstrate that (i) **polymerase** I promoter-binding factor E1BF contains an intrinsic substrate-specific protein kinase and (ii) E1BF is an essential **polymerase** I transcription factor that can modulate rRNA gene transcription by protein phosphorylation. Further, these studies have provided a direct means to identify a protein kinase or any other enzyme that can interact with a specific DNA sequence.

10/3,AB/72 (Item 72 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06652927 91004209 PMID: 2208274
Monomethylated cap structures facilitate **RNA** export from the nucleus.
Hamm J; Mattaj IW
European Molecular Biology Laboratory, Heidelberg, Federal Republic of Germany.
Cell (UNITED STATES) Oct 5 **1990**, 63 (1) p109-18, ISSN 0092-8674 Journal Code: CQ4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
RNA export from the nucleus has been analyzed in Xenopus oocytes. U1 snRNAs made by **RNA polymerase** II were exported into the cytoplasm, while U1 snRNAs synthesized by **RNA polymerase** III, and therefore with a different cap structure, remained in the nucleus. Export of the **polymerase** II-transcribed RNAs was inhibited by the cap **analog** m7GpppG. Spliced mRNAs carrying monomethylguanosine cap structures were rapidly exported, while hypermethylated cap structures delayed mRNA export. The export of a mutant precursor mRNA unable to form detectable splicing complexes was also significantly delayed by incorporation of a hypermethylated cap structure. The results suggest that the m7GpppN cap structure is likely to be a signal for **RNA** export from the nucleus.

10/3,AB/73 (Item 73 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06570204 89193629 PMID: 2930526
5,6-Dichloro-1-beta-D-ribofuranosylbenzimidazole inhibits a HeLa protein kinase that phosphorylates an **RNA polymerase** II-derived peptide.
Stevens A; Maupin MK
Biology Division, Oak Ridge National Laboratory, TN 37831-8077.

Biochemical and biophysical research communications (UNITED STATES) Mar 15 **1989**, 159 (2) p508-15, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A protein kinase that phosphorylates Lys(Tyr-Ser-Pro-Thr-Ser-Pro-Ser)4, a synthetic peptide homologous to the evolutionarily-conserved, tandemly-repeated heptapeptide sequence at the C-terminus of the large subunit of eukaryotic **RNA polymerase** II, has been detected in HeLa cell extracts and chromatographic fractions therefrom. The enzyme, which phosphorylates serine principally, can be distinguished from previously described major protein kinases which phosphorylate the peptide poorly, if at all. It is inhibited by the nucleoside **analog**, 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole. Results suggest that human placental **RNA polymerase** II is phosphorylated at the C-terminus of the large subunit by the partially-purified protein kinase and that the phosphorylation is also sensitive to the nucleoside **analog**.

10/3,AB/74 (Item 74 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06556776 89123297 PMID: 2914905

5,6-Dichloro-1-beta-D-ribofuranosylbenzimidazole inhibits transcription elongation by **RNA polymerase** II in vitro.

Chodosh LA; Fire A; Samuels M; Sharp PA
Department of Biology, Massachusetts Institute of Technology, Cambridge 02139.

Journal of biological chemistry (UNITED STATES) Feb 5 **1989**, 264 (4) p2250-7, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: 5T 32 GM07753-09, GM, NIGMS; P30-CA14051, CA, NCI; PO1-CA42063, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The purine nucleoside **analog** 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole (DRB) is a selective inhibitor of transcription by **RNA polymerase** II. Although a wealth of in vivo studies have suggested that DRB inhibits transcription by enhancing the premature termination of elongating **polymerase** molecules, in vitro studies to date have been interpreted to suggest that DRB acts at the level of transcription initiation. We have analyzed the mechanism of DRB-mediated transcription inhibition in vitro both in HeLa whole cell extracts and in a partially purified transcription system. The results indicate that the extent to which DRB inhibits the synthesis of a **RNA** transcript is directly proportional to its length. For example, DRB was found to preferentially inhibit transcription in vitro of promoter-distal relative to promoter-proximal portions of the adenovirus major late transcription unit. A factor potentially involved in mediating this inhibitory effect is identified. We conclude that the mechanism of DRB inhibition of transcription in vivo and in vitro are similar.

10/3,AB/75 (Item 75 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06430870 88122131 PMID: 3323886

Human acidic ribosomal phosphoproteins P0, P1, and P2: analysis of cDNA clones, in vitro synthesis, and assembly.

Rich BE; Steitz JA
Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, Connecticut 06510-8024.

Molecular and cellular biology (UNITED STATES) Nov **1987**, 7 (11)

p4065-74, ISSN 0270-7306 Journal Code: NGY
Contract/Grant No.: GM 26154, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

cDNA clones encoding three antigenically related human ribosomal phosphoproteins (P-proteins) P0, P1, and P2 were isolated and sequenced. P1 and P2 are **analogous** to Escherichia coli ribosomal protein L7/L12, and P0 is likely to be an **analog** of L10. The three proteins have a nearly identical carboxy-terminal 17-amino-acid sequence (KEESEESD(D/E)DMGFGLFD-COOH) that is the basis of their immunological cross-reactivity. The identities of the P1 and P2 cDNAs were confirmed by the strong similarities of their encoded amino acid sequences to published primary structures of the homologous rat, brine shrimp, and Saccharomyces cerevisiae proteins. The P0 cDNA was initially identified by translation of hybrid-selected mRNA and immunoprecipitation of the products. To demonstrate that the coding sequences are full length, the P0, P1, and P2 cDNAs were transcribed in vitro by bacteriophage T7 **RNA polymerase** and the resulting mRNAs were translated in vitro. The synthetic P0, P1, and P2 proteins were serologically and electrophoretically identical to P-proteins extracted from HeLa cells. These synthetic P-proteins were incorporated into 60S but not 40S ribosomes and also assembled into a complex similar to that described for E. coli L7/L12 and L10.

10/3,AB/76 (Item 76 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06355769 88087036 PMID: 3693365
Purine triphosphate beta-gamma bond hydrolysis requirements for **RNA polymerase** II transcription initiation and elongation.
Rappaport J; Weinmann R
Wistar Institute of Anatomy and Biology, Philadelphia, Pennsylvania 19104.
Journal of biological chemistry (UNITED STATES) Dec 25 **1987**, 262 (36) p17510-5, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: A1-13231, PHS; CA-09171, CA, NCI; CA-10815, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

RNA polymerase II-specific transcription requires, in addition to auxiliary protein factors, the hydrolysis of the beta-gamma phosphate bond of ATP. The nonhydrolyzable **analog** of ATP, imidoadenosine triphosphate does not suffice for specific in vitro transcription (Bunick, D., Zandomeni, R., Ackerman, S., and Weinmann, R. (1982) Cell 29, 877-886), although it can be incorporated into **RNA**. The experiments presented here suggest two energy-dependent steps in **RNA polymerase** II transcription. One of these steps is required at, or close to, the point of initiation, as determined by 5' end primer extension analysis. In vitro transcription occurs efficiently in vitro when imidoadenosine triphosphate is supplemented with dATP to fulfill the energy requirement. In the presence both of imidoadenosine triphosphate and imidoguanosine triphosphate, the concentration of dATP required for transcription initiation is dramatically increased. This suggests that ATP and GTP are co-substrates in transcription initiation, supporting the role of protein kinase II in this process (Zandomeni, R., Zandomeni, M. C., Shugar, D., and Weinmann, R. (1986) J. Biol. Chem. 261, 3414-3419). The concentration of dATP required for maximal initiation is inadequate for the production of full-length transcripts, suggesting a second energy-dependent step in the **RNA** elongation process. Since the elongation step is unaffected by the presence of imidoguanosine triphosphate, GTP beta-gamma phosphate bond hydrolysis appears to be required only for initiation.

10/3,AB/77 (Item 77 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06052217 86187877 PMID: 3697361
Synthetic amatoxin **analogue**. A two-dimensional proton NMR study of S-deoxy-(Ile3)-(D-Ala7)-amaninamide.
Zanotti G; D'Auria G; Paolillo L; Trivellone E
Biochimica et biophysica acta (NETHERLANDS) Apr 22 **1986**, 870 (3) p454-62, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The effect of substitution of L and D amino acids in amatoxin **analogues** is discussed in this paper. The structure of the **analog** where D-alanine substitutes for glycine in position 7 has been worked out in solution by two-dimensional NMR methods using a 500 MHz instrument. The combined use of COSY and NOESY two-dimensional spectra allows a clear assignment of the resonances. The use of the coupling constants permits the calculation of the phi angles of the backbone. The NOE effects reveal the through-space contacts between protons of different peptide units, thus determining the rigidity of the amatoxin structure. On these grounds it has been possible to elucidate the conformation of the amatoxin **analogue** that resembles very closely that of beta-amanitin, thus explaining the high inhibitory activity toward **RNA polymerase** B.

10/3,AB/78 (Item 78 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06002179 90036727 PMID: 2553676
Mutational analysis of the histidine operon promoter of Salmonella typhimurium.
Shand RF; Blum PH; Holzschu DL; Urdea MS; Artz SW
Department of Microbiology, University of California, Davis 95616.
Journal of bacteriology (UNITED STATES) Nov **1989**, 171 (11) p6330-7, ISSN 0021-9193 Journal Code: HH3
Contract/Grant No.: GM27307, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We isolated a collection of 67 independent, spontaneous Salmonella typhimurium his operon promoter mutants with decreased his expression. The mutants were isolated by selecting for resistance to the toxic lactose **analog** o-nitrophenyl-beta-D-thiogalactoside in a his-lac fusion strain. The collection included base pair substitutions. small insertions, a deletion, and one large insertion identified as IS30 (IS121), which is resident on the Mu d1 cts(Apr lac) phage used to construct the his-lac fusion. Of the 37 mutations that were sequenced, 14 were unique. Six of the 14 were isolated more than once, with the IS30 insertion occurring 16 times. The mutations were located throughout the his promoter region, with two in the conserved - 35 hexamer sequence, four in the conserved - 10 hexamer sequence (Pribnow box), seven in the spacer between the - 10 and -35 hexamer sequences, and the IS30 insertions just upstream of the -35 hexamer sequence. Four of the five substitution mutations changed a consensus base pair recognized by E sigma 70 **RNA polymerase** in the -10 or -35 hexamer. Decreased his expression caused by the 14 different his promoter mutations was measured in vivo. Relative to the wild-type promoter, the mutations resulted in as little as a 4-fold decrease to as much as a 357-fold decrease in his expression, with the largest decreases resulting from changes in the most highly conserved features of E sigma 70 promoters.

10/3,AB/79 (Item 79 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05990579 86129357 PMID: 3511843
Spatial relationship between the intrinsic metal in the beta subunit and cysteine-132 in the sigma subunit of Escherichia coli **RNA polymerase**: a resonance energy transfer study.
Chatterji D; Wu CW; Wu FY
Archives of biochemistry and biophysics (UNITED STATES) Jan **1986**, 244 (1) p218-25, ISSN 0003-9861 Journal Code: 6SK
Contract/Grant No.: GM 28069-06, GM, NIGMS; GM28057-03, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Fluorescence excited-state energy transfer measurements were carried out between the N-(1-pyrene)maleimide (PM)-labeled sigma subunit and Co in the beta subunit of Co-Zn **RNA polymerase** (RPase). sigma subunit with or without PM labeling was cleaved with 2-nitro-5-thiocyanobenzoic acid, and the reaction products were analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. One molecule of the fluorescent probe (PM) was found to be attached to the cysteine-132 residue of the sigma subunit. When excited at 340 nm, the fluorescence emission bands from 380 to 420 nm of PM-labeled sigma overlap with the charge transfer absorption band of Co-Zn RPase around 400 nm. Based on Forster's equation, the R0 values for the donor-acceptor pair were calculated to be 21.5 and 22 A in the absence and presence of template **analog** (dA-dT)60, respectively. Using these R0 values and the observed energy transfer efficiencies, the distance between the cysteine-132 of the sigma subunit and Co located at the initiation site of the beta subunit was calculated to be 22 A with or without the template present, indicating that no major conformational change of the enzyme was induced upon template binding. However, a small but significant change in the above distance was observed upon the addition of ATP to RPase in the presence (dA-dT)60 but not in the absence of (dA-dT)60 template. The biological implications of these observations are discussed.

10/3,AB/80 (Item 80 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05975678 90220561 PMID: 2483743
Substrate properties of C'-methylnucleoside triphosphates in a reaction of **RNA** synthesis catalyzed by Escherichia coli **RNA-polymerase**]
Substratnye svoistva C'-metilnukleozidtrifosfatov v reaktsii sinteza RNK, kataliziruemoi RNK-polimerazoi Escherichia coli.
Savochkina LP; Sviriaeva TV; Beigel'man LN; Padiukova NSh; Kuznetsov DA; Lysov IuP; Mikhailov SN; Bibilashvili RSh
Molekuliarnaia biologiia (USSR) Nov-Dec **1989**, 23 (6) p1700-10, ISSN 0026-8984 Journal Code: NGX
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
2 theta-C-methyl substituted and phosphonate **analogs** of UTP were prepared and together with the synthesized earlier 3'-C-methyl-UTP were investigated in the **RNA** synthesis reaction catalysed by Escherichia coli **RNA-polymerase**. Substrate properties of UTP **analogs** were studied in the presence of all natural triphosphates, in the absence of UTP and under conditions of soil substrate reaction. It was shown that UTP(3'CH3) is incorporated into the **RNA** chain and terminates further **RNA** elongation. Another **analog** UTP (2'CH3) may substitute natural UTP in **RNA** synthesis, but the effectivity of its incorporation is diminished. Phosphonate **analog** UTP(5'CH2) is a

pseudoterminator of **RNA** synthesis. The conformational analysis of 2'- and 3'C-methylnucleosides by force-field method of calculation was carried out in order to find energetically forbidden conformations of these **analogs** due to the collision of bulky methyl group and a heterocyclic base. An attempt was made to fix the conformation of the substrate during its enzymatic transformation.

10/3,AB/81 (Item 81 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05949711 89271831 PMID: 2854956
Antiviral activity and mode of action of ribavirin 5'-sulfamate against Semliki Forest virus.
Smee DF; Alaghamandan HA; Kini GD; Robins RK
Nucleic Acid Research Institute, Costa Mesa, California 92626.
Antiviral research (NETHERLANDS) Dec 11 **1988**, 10 (6) p253-62, ISSN 0166-3542 Journal Code: 6I7
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Ribavirin 5'-sulfamate, a nucleotide **analog** , inhibited Semliki Forest virus cytopathology by 50% at 10 microM, whereas ribavirin was inactive at less than or equal to 1 mM. Actinomycin D did not reverse (antagonize) the effect of ribavirin 5'-sulfamate against the virus. The compound inhibited amino acid incorporation into macromolecules of uninfected cells but had no appreciable effect on uridine incorporation. Infected cells treated with actinomycin D and nucleotide **analog** were inhibited in amino acid and uridine incorporation. The compound blocked the formation of the viral **RNA polymerase** protein in cells, which could account for the inhibited synthesis of new viral **RNA**. By electrophoresis, inhibition of the synthesis of viral proteins was more pronounced than the inhibition of cellular polypeptides. The **analog** inhibited the translation of mRNA to protein. Most animals treated intraperitoneally for 7 days with ribavirin 5'-sulfamate at 20 and 40 mg/kg/day starting 2 h before intraperitoneal Semliki Forest virus inoculation survived the otherwise lethal infection.

10/3,AB/82 (Item 82 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05942724 89382764 PMID: 2476568
Identification of factors specific for transcription of the late class of vaccinia virus genes.
Wright CF; Moss B
National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892.
Journal of virology (UNITED STATES) Oct **1989**, 63 (10) p4224-33 , ISSN 0022-538X Journal Code: KCV
Contract/Grant No.: GM 10958, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cytoplasmic extracts made from HeLa cells that have been harvested late after infection with vaccinia virus are capable of specifically transcribing templates containing vaccinia virus late-gene promoters. We applied such an extract to a phosphocellulose column and eluted the proteins with a series of buffers containing successively higher concentrations of NaCl. None of three column fractions alone was capable of specific transcription of a late-gene template. However, specific transcriptase activity could be reconstituted by mixing column fractions, with maximal activity seen when all three fractions were present. The activities present in all fractions were heat labile, resistant to

micrococcal nuclease, and present only in extracts from vaccinia virus-infected cells. A quantitative complementation assay was used to further purify one factor, named VLTF-1, over subsequent columns of DEAE-cellulose and hydroxylapatite. VLTF-1 was separated from endogenous **RNA polymerase** , was a late-promoter-specific transcription factor, and had a sedimentation rate consistent with an apparent Mr of 45,000. The **RNA polymerase** -containing fraction was not only necessary for transcription with a late-promoter template but alone was capable of specifically transcribing a vaccinia virus early-gene promoter. A further difference between early and late gene transcription in this system was in the ability of the ATP **analog** beta-8-imidoadenosine-5'-triphosphate (AMP-PNP) to substitute for ATP in supporting specific transcription of only the late-promoter template. The system reconstituted from the various fractions retained the ability to produce the novel poly(A) sequence found on the 5' end of vaccinia virus late messages.

10/3,AB/83 (Item 83 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05942603 89380068 PMID: 2550417
Lack of CSF-1 receptor message in Reed-Sternberg cells.
Farhi DC
Institute of Pathology, Case Western Reserve University, Cleveland, Ohio 44106.
Hematologic pathology (UNITED STATES) **1989**, 3 (2) p85-90,
ISSN 0886-0238 Journal Code: HEH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The histogenesis of the Reed-Sternberg (R-S) cell in Hodgkin's disease is uncertain. Some have suggested that it is a derivative of the monocyte/macrophage lineage. To explore this possibility, we have searched for the presence of mRNA corresponding to the c-fms proto-oncogene, a marker for cells of the monocyte/macrophage lineage which encodes the colony-stimulating factor-1 receptor. In situ hybridization was performed using a single-stranded c-fms complementary **RNA** (cRNA) to probe R-S cells, lymphocytes, and eosinophils from touch imprints of a lymph node from a 12-year-old boy with mixed cellularity Hodgkin's disease in relapse. The probe was synthesized from a bacterial plasmid, pSM3, into which a portion of v-fms (a viral-derived oncogene) had been inserted. The plasmid was linearized with a restriction endonuclease, and 35S-labeled cRNA was synthesized from the DNA template using T3 **RNA polymerase** and the nucleotide **analog** [35S]UTP. Positive control hybridizations were obtained with the human acute promyelocytic cell line HL-60 induced to monocyte differentiation. R-S cells were clearly negative, supporting a cell of origin other than the monocyte. In situ hybridization is a potentially powerful method for exploring differentiation and assigning cell lineage in R-S cells.

10/3,AB/84 (Item 84 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05923576 89024476 PMID: 3052250
Mechanistic studies on N-benzyladriamycin-14-valerate (AD 198), a highly lipophilic alkyl adriamycin **analog**.
Lameh J; Chuang LF; Israel M; Chuang RY
Department of Pharmacology, School of Medicine, University of California, Davis 95616.
Anticancer research (GREECE) Jul-Aug **1988**, 8 (4) p689-93,
ISSN 0250-7005 Journal Code: 59L
Contract/Grant No.: CA 33022, CA, NCI; CA 37082, CA, NCI

Languages: ENGLISH
Document type: Journal Article
Record type: Completed
AD 198, a novel lipophilic N-alkyl derivative of adriamycin (ADR) and a potential anticancer agent for preclinical development, was studied for its effects on the activities of DNA and **RNA polymerases** in vitro and its ability to bind DNA. AD 198, which contains a benzyl substituent on the glycosidic amine, was found to interact with DNA through drug-DNA binding to an extent less than its parent compound ADR as shown by fluorescent emission spectra studies. It had a preferential inhibitory effect against **RNA** vs. DNA synthesis in vitro by **RNA** or DNA **polymerases** from both E. coli and chicken leukemia cells. Preincubation studies indicated that AD 198 may inhibit the activity of E. coli **RNA polymerase** through drug-template interaction and that of leukemic **RNA polymerase**, which uses single stranded DNA as template, through enzyme inactivation.

10/3,AB/85 (Item 85 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05913275 88134253 PMID: 2449209
Characterization of a photoaffinity **analog** of UTP, 5-azido-UTP for analysis of the substrate binding site on E. coli **RNA polymerase**.
Woody AY; Evans RK; Woody RW
Department of Biochemistry, Colorado State University, Fort Collins 80523.
Biochemical and biophysical research communications (UNITED STATES) Feb 15 **1988**, 150 (3) p917-24, ISSN 0006-291X Journal Code: 9Y8
Contract/Grant No.: GM-23697, GM, NIGMS; GM-35766, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The substrate binding site on E. coli **RNA polymerase** was investigated by photoaffinity labeling with a photoaffinity **analog** of UTP, 5-azido-UTP. We have established that 5-azido-UTP is a substrate for **RNA polymerase** by specific transcription on 229 bp DNA containing the gene II promoter of M13 phage. Analysis of the initial rate of **RNA** synthesis gives Km(5-azido-UTP) approximately 80 microM. Photolabeling with varying concentrations of 5-azido-UTP follows a saturation curve with the midpoint occurring at a 5-azido-UTP concentration of 65 microM near to the Km obtained by kinetic analysis. 5-Azido-UTP photolabels the beta', beta, and sigma subunits to about the same extent, both in the presence (33, 31, and 36%) and absence (35, 30 and 35%) of DNA. This labeling pattern is somewhat different from that obtained with 8-azido-ATP (beta' greater than sigma much greater than beta greater than alpha).

10/3,AB/86 (Item 86 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05904753 88013811 PMID: 2443829
5'-C-methylnucleoside triphosphates in the reaction of **RNA** synthesis catalyzed by Escherichia coli **RNA-polymerase**]
5'-C-methylnukleozidtrifosfaty v reaktsii sinteza RNK, kataliziruemoi RNK-polimerazoi Escherichia coli.
Aivazashvili VA; Mikhailov SN; Padiukova NSh; Bibilashvili RSh; Karpeiskii MIa
Molekuliarnaia biologiia (USSR) Jul-Aug **1987**, 21 (4) p1080-91, ISSN 0026-8984 Journal Code: NGX
Languages: RUSSIAN
Document type: Journal Article

Record type: Completed
It was shown that **RNA-polymerase** is able to discriminate diastereoisomers of 5'-methyl-substituted **analogs** of ribonucleoside triphosphates (rNTP). Under conditions of soil substrate reactions when the **analog** is added to the presynthesized ternary complexes, D-allo- and L-talo-stereoisomers incorporate into **RNA** 100 and 1000 times, respectively, less effectively, then the natural rNTP. The effectivities of incorporation of other 2'- and 3'-substituted **analogs** of rNTP were measured under the same conditions and compared with that for 5'-Me-rNTP. It was shown also that **RNA-polymerase** does not support long-chain **RNA** synthesis from 5'-Me-rNTP in the absence of natural rNTP. No more then two **analog** residues can be attached to the 3'-end of the presynthesized **RNA** under such conditions. Addition of one natural rNTP to this reaction mixture results in the synthesis of long alternating **RNA** containing D-allo-stereoisomer and natural rNTP residues. In the case of L-talo-stereoisomer **RNA** elongation is not inhibited, if the distance between the **analog** residues in the **RNA** chain is not shorter then five nucleotide residues. The rate of pyrophosphorolysis from the **RNA** of the **analogs** studied was the same as for the natural rNTP residues.

10/3,AB/87 (Item 87 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05900635 87257810 PMID: 3299044
Kinetics of inhibition by 8-oxy-ATP of the dinucleotide pppApU synthesis catalyzed by Escherichia coli **RNA-polymerase** on the promoter A1 of phage T7 delta D111 DNA during coupled synthesis of di- and trinucleotides and a limited set of substrates]
Kinetika ingibirovaniia 8-oksi-ATP sinteza dinukleotida pppApU RNK-polimerazoi Escherichia coli na promotore A1 DNK faga T7 delta D111 v usloviiakh sopriazhennogo sinteza di- i trinukleotida i ogranichennogo nabora substratov.
Kuriavyi VV; Bruskov VI
Molekuliarnaia biologiia (USSR) Mar-Apr **1987**, 21 (2) p462-71, ISSN 0026-8984 Journal Code: NGX
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
A kinetic analysis of inhibition of synthesis of dinucleotide pppApU catalyzed by Escherichia coli **RNA-polymerase** on A1 promoter of the DNA from T7 delta DIII phage mutant by 8-oxy-ATP under the conditions of the coupled synthesis of pppApU and pppApUpC and in the presence of an incomplete set of substrates, namely ATP, UTP, CTP, has been performed. It was found that 8-oxy-ATP is an unproductive **analog** of both ATP and CTP. A comparative analysis of the dissociation constants shows that 8-oxy-ATP binds at ATP center 3.3. times and at CTP center 540 times weaker than natural substrates. At the UTP center 8-oxy-ATP does not bind at all.

10/3,AB/88 (Item 88 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05896087 87156723 PMID: 3548721
Characterization of the guanosine-3'-diphosphate-5'-diphosphate binding site on E. coli **RNA polymerase** using a photoprobe, 8-azidoguanosine-3'-5'-bisphosphate.
Owens JR; Woody AY; Haley BE
Biochemical and biophysical research communications (UNITED STATES) Feb 13 **1987**, 142 (3) p964-71, ISSN 0006-291X Journal Code: 9Y8
Contract/Grant No.: GM-23697? GM-35766, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article

Record type: Completed
Nucleotide binding sites on DNA-dependent **RNA polymerase** from E. coli have been studied by photoaffinity labeling with a GTP **analog** [gamma-32P]-8-AzidoGTP and a guanosine-3'-diphosphate-5'-diphosphate **analog**, 8-Azidoguanosine-3'-phosphate-5'-85'-32P]phosphate. The guanosine diphosphate photoprobe labeled the beta, beta', and sigma subunits with the sigma subunit being most heavily labeled. The GTP photoprobe also labeled the beta, beta', sigma subunits but the beta' subunit was most heavily labeled. In competition experiments guanosine-3'-diphosphate-5'-diphosphate decreased photolabeling by 8-Azidoguanosine-3'-phosphate-5'-[5'-32P]phosphate better than GTP, while the opposite was true for photolabeling with [gamma-32P]8- AzidoGTP. The guanosine diphosphate photoprobe inhibited transcription on E. coli DNA with Ki of ca. 150 microM. Present studies suggest a unique ppGpp binding site distinct from substrate binding site(s) and this photoprobe may be used to localize this binding site(s).

10/3,AB/89 (Item 89 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05894030 87109196 PMID: 2948952
DNA functional groups required for formation of open complexes between Escherichia coli **RNA polymerase** and the lambda PR promoter. Identification via base **analog** substitutions.
Dubendorff JW; deHaseth PL; Rosendahl MS; Caruthers MH
Journal of biological chemistry (UNITED STATES) Jan 15 **1987**, 262 (2) p892-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM21120, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Synthetic 75-base pair promoters bearing base changes and/or base **analog** substitutions at selected positions were constructed. Using both abortive initiation and run-off transcription assays, the interaction of these altered promoters with Escherichia coli **RNA polymerase** was studied in order to determine the involvement of DNA functional groups in promoter recognition. Two adjacent thymines in the -35 region were identified whose 5-methyl groups play a crucial role. Additionally, the combined results from several substitution experiments showed that functional groups in the major groove of the strongly conserved T-A base pair at the -7 position are probable sites of direct interaction with **RNA polymerase**.

10/3,AB/90 (Item 90 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05892183 87064626 PMID: 3785224
Rapid enrichment of HeLa transcription factors IIIB and IIIC by using affinity chromatography based on avidin-biotin interactions.
Kasher MS; Pintel D; Ward DC
Molecular and cellular biology (UNITED STATES) Sep **1986**, 6 (9) p3117-27, ISSN 0270-7306 Journal Code: NGY
Contract/Grant No.: AI-19973, AI, NIAID; CA-16038, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Plasmid DNA containing the adenovirus type 2 genes for VA **RNA** was linearized at a site distal to the gene, end labeled with a biotin-nucleotide **analog** of TTP, and incubated with avidin to form an avidin-biotinylated DNA complex. HeLa cell S100 extracts containing crude **RNA polymerase** III and transcription factors (TFs) IIIB and IIIC were programmed with the avidin-biotin-VA DNA to allow stable complex

formation (A.B. Lassar, P.L. Martin, and R.G. Roeder, Science 222:740-748, 1983). Chromatography of the programmed extract over a biotin-cellulose affinity resin resulted in the selective, and virtually quantitative, retention of one of two stable preinitiation complexes, either VA-IIIC or VA-IIIC-IIIB, depending on the length of template incubation in the S100 extract. After washing the resin with 0.10 M and 0.25 M KCl to remove **RNA polymerase** III and nonspecifically bound proteins, respectively, TFIIIC was eluted from the VA-IIIC complex by the addition of 1.5 M KCl. The VA-IIIC-IIIB complex exhibited a higher salt stability. Most of TFIIIB and some TFIIIC were released by the addition of 1.5 M KCl; however, the majority of TFIIIC activity was recovered only after a subsequent 3.0 M KCl elution. The specific activity of the TFIIIC in the 3.0 M KCl fraction was 770-fold higher than that in the S100 extract, while the protein content of the 1.5 and 3.0 M KCl fractions was reduced 7,500- and 100,000-fold, respectively.

10/3,AB/91 (Item 91 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05881240 86221709 PMID: 2423415
Construction and characterization of pBR322-derived plasmids with deletions of the **RNA** I region.
Gayle RB; Vermersch PS; Bennett GN
Gene (NETHERLANDS) **1986**, 41 (2-3) p281-8, ISSN 0378-1119
Journal Code: FOP
Contract/Grant No.: GM26437, GM, NIGMS; GMO7833, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A region upstream from the origin of replication in ColE1-type plasmids has been shown to be necessary for replication. Two **RNA** transcripts are produced from this area, **RNA** II, which yields the primer for DNA **polymerase** initiation at the origin and **RNA** I, which is complementary to the 5' end of **RNA** II and acts to inhibit primer formation. We have constructed plasmids which do not possess the nucleotide sequence for **RNA** I, or the normal 5' terminus and promoter of **RNA** II. The **RNA** II **analog**, in these plasmids, is believed to be synthesized by the readthrough transcription of the upstream trimethoprim-resistant dihydrofolate reductase (DHFR) gene at a level comparable to that produced by the tryptophan promoter. These plasmids have a copy number of about tenfold higher than that of pBR322 during logarithmic growth and are compatible with other ColE1-type plasmids. These plasmids are stably maintained in several strains when selective pressure is present and the plasmids are stably maintained during exponential growth in W3110 strains without selective pressure. In all strains examined, the dimeric form of the plasmid was lost from cells much more rapidly than those containing the monomeric form.

10/3,AB/92 (Item 92 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05880890 86214031 PMID: 2423030
Synthesis and properties of adenosine-5'-triphosphoro-gamma-1-(5-sulfonic acid)naphthyl ethylamidate: a fluorescent nucleotide substrate for DNA-dependent **RNA polymerase** from Escherichia coli.
Wu FY; Abdulwajid AW; Solaiman D
Archives of biochemistry and biophysics (UNITED STATES) May 1 **1986**, 246 (2) p564-71, ISSN 0003-9861 Journal Code: 6SK
Contract/Grant No.: 1F32ESO5254-01, ES, NIEHS; GM-28057-03, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A new fluorescent ATP **analog**, adenosine-5'-triphosphoro-gamma-1-(5-sulfonic acid)naphthyl ethylamidate (gamma-1,5-EDANS)ATP, containing the fluorophore N-(aminoethyl)-5-naphthylamine-1-sulfonic acid attached via a gamma-phosphoamidate bond was synthesized in good yield. It has absorption maxima at 255 and 344 nm and a fluorescence emission maximum at 490 nm. These spectral characteristics permit its uses as an energy acceptor for energy transfer from the intrinsic protein fluorophores and as an energy donor for the energy transfer to the intrinsic Co of Co-substituted **RNA polymerases**. This **analog** is a good substrate for Escherichia coli **RNA polymerase** and can be used to initiate the **RNA** chain. Incorporation of this **analog** into the total **RNA** synthesized was about 60% of that observed for ATP, independent of the templates used. Its Km values (22 and 118 microM) are twofold higher and its Vmax values (45 and 59 nmol/min/mg of enzyme) are 40% lower than those for ATP using calf thymus DNA and poly[d(A-T)], respectively, as template. For abortive initiation reaction using pAR1435 plasmid DNA as template, the Km and Vmax values of this **analog** are 2.7 times higher and 7 times lower, respectively, than those of ATP. With its desirable spectroscopic properties, (gamma-1,5-EDANS)ATP is a good probe for the studies of nucleotide-protein interactions, active site mapping of **RNA polymerase**, and other ATP-utilizing biological systems.

10/3,AB/93 (Item 93 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05716452 85226616 PMID: 2988649
Kinetics of the interaction of methylene diphosphonic acid and inorganic pyrophosphate with DNA-dependent **RNA-polymerase** from calf thymus]
Kinetika vzaimodeistviia metilendifosfonovoi kisloty i neorganicheskogo pirofosfata s DNK-zavisimoi RNK-polimerazoi II timusa telenka.
Fomovskaia GN; Komissarenko SV
Biokhimiia (USSR) May **1985**, 50 (5) p839-43, ISSN 0320-9725
Journal Code: A28
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
The kinetics of interaction of PPi and its diphosphonic **analog**, methylenediphosphonic acid (MDPA), with nucleoside triphosphates, DNA and Mg2+ binding sites of DNA-dependent **RNA polymerase** II from calf thymus was investigated. The values of apparent Km in the NTP polymerization reaction for ATP and CTP equal to 2.7 X 10(-4) and 1.8 X 10(-4) M, respectively, were determined. It was shown that MDPA and PPi competitively inhibited the **RNA polymerase** reaction with respect to nucleoside triphosphate. The inhibition constants (Ki) of ATP and CTP incorporation for MDPA were 2.2 X 10(-4) and 3.3 X 10(-4) M, respectively, while those of the nucleoside triphosphate incorporation for PPi were equal to 1.4 X 10(-4) and 2.0 X 10(-4) M, respectively. MDPA and PPi were incompetitive inhibitors of template (DNA) and Mn2+. A possible mechanism of inhibition of the **RNA polymerase** reaction by MDPA is proposed.

10/3,AB/94 (Item 94 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05626460 87031218 PMID: 3095161
A Drosophila melanogaster mutant resistant to a chemical **analog** of juvenile hormone.
Wilson TG; Fabian J
Developmental biology (UNITED STATES) Nov **1986**, 118 (1) p190-201, ISSN 0012-1606 Journal Code: E7T
Languages: ENGLISH

Document type: Journal Article
Record type: Completed

Methoprene, a chemical **analog** of juvenile hormone, is toxic when applied to late third-instar larvae of Drosophila melanogaster. Using an ethyl methane sulfonate mutagenesis screen, we have selected two noncomplementing mutants, one of which is nearly 100 times more resistant than wild-type to either methoprene or juvenile hormone III topically applied or incorporated into the diet. The mutation, named methoprene-tolerant (Met), also confers resistance to methoprene-induced pseudotumor formation in larvae as well as to juvenile hormone III- or methoprene-induced vitellogenic oocyte development in adult females. Met adults show little or no cross-resistance to four other insecticides. The mutation was mapped by recombination to a location 35.4 on the X-chromosome and uncovered by chromosomes deficient for the region 10C2-10D4. Complementation was observed between Met and a lethal allele of the **RNA polymerase** II locus, which is also found in this region.
Since the Met mutation also confers resistance to methoprene-induced abnormalities in adult cuticle formation, the autonomy of Met expression could be evaluated in flies mosiac for this mutation. Autonomous expression of Met was found both in abdominal cuticle as well as in external male genitalia. The characteristics of Met are consistent with those expected of a mutant having altered juvenile hormone reception in target tissue.

10/3,AB/95 (Item 95 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05356217 90093668 PMID: 2599760

Structure-toxicity relationships in the amatoxin series. Synthesis of S-deoxy[gamma(R)-hydroxy-Ile3]-amaninamide, its crystal and molecular structure and inhibitory efficiency.

Zanotti G; Wieland T; Benedetti E; Di Blasio B; Pavone V; Pedone C
Department of Pharmaceutical Studies, University La Sapienza, Rome, Italy.

International journal of peptide and protein research (DENMARK) Sep **1989**, 34 (3) p222-8, ISSN 0367-8377 Journal Code: GSD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The amatoxins, highly toxic components of Amanita mushrooms, strongly inhibit the DNA-dependent **RNA polymerase** II (or B) in eukaryotic cell nuclei. For optimal binding to the enzyme a gamma-hydroxyisoleucine side chain in the 3-position is important as in gamma-amanitin (compound 1), where the OH-group is bound in the [S]-configuration. Amanullin, a non-toxic component, having an oxygen-free isoleucine side chain no. 3, exhibits an inhibitory effect on **RNA polymerase** II about two orders of magnitude smaller than that of gamma-amanitin. An equal, relatively weak, inhibitory effect has previously been found with the synthetically obtained Ile3-**analog** 7. In the present paper the synthesis of an **analog** (2) bearing a gamma-hydroxyl group in the isoleucine side chain is described. The compound was found to have about the same inhibitory effect on **RNA polymerase** II from Drosophila embryos as amanullin and the Ile3-**analog** 7. Structure analysis by X-ray diffraction revealed that the hydroxyl group at the -carbon atom of side chain-3 has the [R]-configuration, the new **analog** thus being -deoxo[( )-hydroxy-[Ile3]-amaninamide. It follows that the [S]-configuration of this chiral center is a prerequisite to maximal toxicity. Crystallographic data demonstrating great similarity between the peptide backbones of the new **analog** and those of natural amatoxins are given.

10/3,AB/96 (Item 96 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05200059 88206076 PMID: 3363868
Effect of inhibitors of the host cell **RNA polymerase** II on African swine fever virus multiplication.
Salas J; Salas ML; Vinuela E
Centro de Biologia Molecular (CSIC-UAM), Facultad de Ciencias, Universidad Autonoma Canto Blanco, Madrid, Spain.
Virology (UNITED STATES) May **1988**, 164 (1) p280-3, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The role of the host cell **RNA polymerase** II in African swine fever (ASF) virus growth has been examined using inhibitors of this enzyme. The adenosine **analog** 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole (DRB), an inhibitor of mRNA precursor synthesis in mammalian cells, strongly inhibits the production of infectious progeny virus in Vero cells, but does not significantly affect the synthesis of virus-specific macromolecules. On the other hand, virion assembly seems to proceed normally in the presence of DRB, as virus particles can be seen in electron micrographs with a morphology indistinguishable from that observed in the absence of the inhibitor. However, taking into account the inhibition of the infectivity caused by the drug, most of these particles must be defective. In contrast with this effect of DRB on ASF virus replication, the toxin alpha-amanitin does not inhibit the production of infectious ASF virus in Vero cells or porcine alveolar macrophages. This result indicates that the host **RNA polymerase** II does not transcribe viral genes and that active transcription of the cell genome is not needed for ASF virus replication.

10/3,AB/97 (Item 97 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04874353 84026497 PMID: 6313215
Topological linkage of circular DNA molecules promoted by Ustilago rec 1 protein and topoisomerase.
Kmiec EB; Kroeger PE; Brougham MJ; Holloman WK
Cell (UNITED STATES) Oct **1983**, 34 (3) p919-29, ISSN 0092-8674 Journal Code: CQ4
Contract/Grant No.: GM 27103, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We studied the formation of linked circular DNA molecules promoted by the combined action of rec 1 protein and type I topoisomerase of Ustilago maydis. When ATP was added as cofactor to reactions containing rec 1 protein, pairs of homologous circular DNA molecules became linked after addition of topoisomerase. Closed circular duplex molecules could be joined at homologous sites with circular single-stranded molecules or with other circular duplex molecules, provided that homologous single-stranded DNA fragments or **RNA polymerase** and nucleoside triphosphates were also added. Complexes formed were topologically linked through regions of heteroduplex DNA. When the **analog** adenylyl-imidodiphosphate was substituted for ATP, nonhomologous pairs of circular DNA molecules became linked.

10/3,AB/98 (Item 98 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04855672 81074352 PMID: 6777632
Nucleotide sequence of a promoter recognized by Bacillus subtilis **RNA polymerase**.

Lee G; Talkington C; Pero J
Molecular & general genetics (GERMANY, WEST) **1980**, 180 (1) p57-65, ISSN 0026-8925 Journal Code: NGP
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We report the nucleotide sequence of a promoter recognized by **RNA polymerase** from the gram-positive bacterium Bacillus subtilis. This promoter, which was isolated from B. subtilis phage SP01 DNA, is homologous to promoters for Escherichia coli **RNA polymerase**; the sequences of the "-35 region" and the "Pribnow box" were 5'TTGACT and 5'CATAAT, respectively (T is the thymine **analog** 5-hydroxymethyluracil in SP01 DNA). These sequences each differed by only a single base pair from the preferred sequences for E. coli promoters. Not surprisingly, the SP01 promoter was actively transcribed in vitro by E. coli **RNA Polymerase** as well as by B. subtilis **RNA polymerase**.

10/3,AB/99 (Item 99 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04844096 81191938 PMID: 6262327
Mechanism of dnaB protein action. IV. General priming of DNA replication by dnaB protein and primase compared with **RNA polymerase**.
Arai K; Kornberg A
Journal of biological chemistry (UNITED STATES) May 25 **1981**, 256 (10) p5267-72, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The general priming system of dnaB protein and primase (Arai, K., and Kornberg, A. (1979) Proc. Natl. Acad. Sci. U. S. A. 76, 4308-4312) when compared with priming by **RNA polymerase** shows a number of striking differences. The general priming system is initiated primarily at single-stranded region(S), being active only on single-stranded DNAs (phages and homopolymers) and inhibited by single-stranded DNA binding protein (SSB). Transcripts are only 10 to 60 residues long. By contrast, **RNA** priming by **RNA polymerase** is initiated at base-paired regions that are not destabilized by SSB (Geider, K., Beck, E., and Schaller, H. (1978) Proc. Natl. Acad. Sci. U. S. A. 76, 645-649) and transcripts on DNA not coated with SSB are generally longer. In general priming, ATP (or GTP) has three functions: (i) an allosteric effect on dnaB protein in which the nonhydrolyzed **analogs** adenosine-5'-O-(3'-thiotri phosphate) (or guanosine-5'-O-(3'-thiotriphosphate) can substitute, (ii) initiation of primer synthesis which can incorporate deoxy-, as well as ribonucleotides, and (iii) elongation of the primer, in which the beta, gamma-imido **analog** can replace ATP (or GTP). An allosteric effect of ATP on **RNA polymerase** has not been demonstrated, nor has the facile synthesis of hybrid transcripts of ribo- and deoxyribonucleotides.

10/3,AB/100 (Item 100 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04843451 81174722 PMID: 7012794
Rho-independent termination: dyad symmetry in DNA causes **RNA polymerase** to pause during transcription in vitro.
Farnham PJ; Platt T
Nucleic acids research (ENGLAND) Feb 11 **1981**, 9 (3) p563-77, ISSN 0305-1048 Journal Code: O8L
Contract/Grant No.: 5T3207223-06, PHS; GM22830, GM, NIGMS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Termination of transcription by **RNA polymerase** at rho-independent sites appears to depend primarily upon two structural features, a region of GC-rich dyad symmetry in the DNA preceding the stop point and a stretch of uridines at the 3' end of the transcript. The possibility that the former might be responsible for slowing elongation prompted us to perform a kinetic analysis of transcription across the leader and terminator regions of the E. coli tryptophan (trp) operon. Regions where the elongation rate is dramatically slowed or stopped are identifiable because they generate discrete transcript hands on a gel. Species derived from pause sites, unlike those resulting from termination sites, are transient and detectable only within the first two minutes of transcription, since **polymerase** eventually resumes elongation. At two mutant trp attenuator sites (trp a135 and trp a1419), where termination is incomplete or absent in vitro, a substantial pause is nevertheless observed. Likewise, a significant pause occurs at trp t, the termination site at the end of the operon. Our experiments also reveal a major pause site at about position 90 in the trp leader sequence, just past a region of dyad symmetry. The **RNA** hairpin corresponding to this site is U-rich, and pausing is strongly enhanced by incorporation of BrUTP. In contrast, this **analog** does not affect pausing at the attenuator or terminator sites with hairpins that are GC-rich. These results strongly support the hypothesis that pausing of the **polymerase** is an obligatory prelude to rho-independent termination. Moreover, the termination event evidently results from consecutive but discrete responses to separate structural features of these sites.

10/3,AB/101 (Item 101 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04839668 81074761 PMID: 6160396
N4-hydroxycytidine: a mutagen specific for AT to GC transitions.
Janion C; Glickman BW
Mutation research (NETHERLANDS) Aug **1980**, 72 (1) p43-7, ISSN 0027-5107 Journal Code: NNA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
N4-Hydroxycytidine is a mutagen of the base-**analog** type and one of the products formed by treatment of cytidine with hydroxylamine. In this communication evidence is presented showing that, in contrast with other known base **analogs** , N4-hydroxycytidine results mainly, if not exclusively, in AT leads to GC transitional alterations in Escherichia coli K12.

10/3,AB/102 (Item 102 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04835429 80227607 PMID: 6156150
2'-Deoxy-2'-azidoadenosine triphosphate and 2'-deoxy-2'-fluoroadenosine triphosphate as substrates and inhibitors for Escherichia coli DNA-dependent **RNA polymerase**.
Ishihama A; Enami M; Nishijima Y; Fukui T; Ohtsuka E; Ikehara M
Journal of biochemistry (JAPAN) Mar **1980**, 87 (3) p825-30, ISSN 0021-924X Journal Code: HIF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The effects of 2'-substitutions of ATP on the substrate and inhibitor properties for **RNA** synthesis were studied in the poly(dAT)-dependent reaction of Escherichia coli **RNA polymerase**. In the presence of UTP, 2'-deoxy-2'-azidoadenosine 5'-triphosphate (AZTP) was incorporated into an acid-insoluble fraction at one-tenth of the rate of ATP

incorporation; it thus acts as a competitive inhibitor for poly(AU) synthesis. On the other hand, another ATP **analog** , 2'-deoxy-2'-fluoroadenosine 5'-triphosphate (AfTP), was co-polymerized with UTP into acid-insoluble materials at a rate less than 1% of that of ATP incorporation; in addition, it exerted a strong but mixed-type inhibition on poly(AU) synthesis. Different modes of action of the two ATP **analogs** are discussed in connection with the specificity of substrate recognition by **RNA polymerase**.

10/3,AB/103 (Item 103 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04820706 84239811 PMID: 6203910
Synthesis of human U1 **RNA**. II. Identification of two regions of the promoter essential for transcription initiation at position +1.
Skuzeski JM; Lund E; Murphy JT; Steinberg TH; Burgess RR; Dahlberg JE
Journal of biological chemistry (UNITED STATES) Jul 10 **1984**, 259 (13) p8345-52, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have analyzed the requirements for human U1 **RNA** transcription catalyzed by **RNA polymerase** II. In Xenopus laevis oocytes, a human U1 **RNA** gene with only 231 and 35 nucleotides of the 5' and 3' flanking regions, respectively (Lund, E. and Dahlberg, J. E. (1984) J. Biol. Chem. 259, 2013-2021), is able to support accumulation of human U1 **RNA** . We show that the point in the template corresponding to the 5' end of U1 **RNA** is a site of transcription initiation. That result rules out the possibility that the 5' end of U1 **RNA** is generated by cleavage and capping of a precursor **RNA** . The accumulation of correctly initiated human U1 **RNA** transcripts requires at least two essential upstream elements. The region between positions -231 and -203 is indispensable for transcription both in oocytes and in vitro. The other region, between positions -105 and -6, fixes the location of the 5' ends of the U1 **RNA** transcripts in oocytes while not altering the overall level of transcription. This latter region contains a sequence located around position -50, which we propose serves as the **analog** of the T-A-T-A sequence in U1 and U2 **RNA** genes.

10/3,AB/104 (Item 104 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04586874 85054970 PMID: 6501318
Inhibitory effect of 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole on a protein kinase.
Zandomeni R; Weinmann R
Journal of biological chemistry (UNITED STATES) Dec 10 **1984**, 259 (23) p14804-11, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: A-21124, PHS; AI-13231, AI, NIAID; CA-10815, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The adenosine **analog** 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole (DRB) inhibits specific in vitro transcription initiation by **RNA polymerase** II. We report here that DRB inhibits a protein kinase present in an extract of HeLa cells and does not inhibit other protein kinases contained in the same extract. The protein kinase affected by DRB is cyclic AMP independent, prefers acidic protein substrates such as casein and phosvitin, and utilizes GTP as the phosphate donor almost as effectively as ATP in the phosphotransferase reaction. The DRB-sensitive protein kinase is also stimulated by polyamines and inhibited by quercitin and heparin. The biochemical and chromatographic properties of this enzyme

correspond to those characteristic of casein kinase II. In HeLa cells, DRB is able to inhibit in vivo phosphorylation on some nuclear proteins. In HeLa cell extracts, in vitro phosphorylation of several proteins by [gamma-32P]GTP is inhibited by DRB. This protein kinase has a DRB sensitivity profile identical to the one previously reported for specific in vitro transcription by **RNA polymerase** II in a whole-cell extract (Zandomeni, R., Mittleman, B., Bunick, D., Ackerman, S., and Weinmann, R. (1982) Proc. Natl. Acad. Sci. U.S.A. 79, 3167-3170). Thus we suggest that this protein kinase mediates DRB inhibition of specific **RNA polymerase** II transcription in vivo and in vitro.

10/3,AB/105 (Item 105 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04554110 84185651 PMID: 6715344
Energy requirement for specific transcription initiation by the human **RNA polymerase** II system.
Sawadogo M; Roeder RG
Journal of biological chemistry (UNITED STATES) Apr 25 **1984**, 259 (8) p5321-6, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: CA 24223-01, CA, NCI; CA 24891-01, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The energy requirement for specific transcription initiation and elongation by the human **RNA polymerase** II system was studied in vitro using partially purified transcription factors from HeLa cell nuclear extracts. The synthesis of the 536-nucleotide long run-off transcript resulting from initiation at the adenovirus major late promoter was found to be dependent upon the presence of either ATP or dATP (with the imido derivative adenyl-5'-yl imidodiphosphate being used as the substrate for the **RNA polymerase** elongation reaction). An identical requirement for hydrolysis of the phosphate bond in an adenosine nucleotide was observed for the synthesis of the decanucleotide transcribed from the major late promoter in the absence of the GTP substrate. In contrast, the nonhydrolyzable **analog** adenyl-5'-yl imidodiphosphate fully substitutes for ATP during the subsequent elongation of these short transcripts, which demonstrates that the energy requirement occurs at an earlier step of the transcription reaction. Thus the particular transcription factor that requires ATP (or dATP) hydrolysis for its function must act prior to, or concomitant with, formation of the first few phosphodiester linkages by the **RNA polymerase** II.

10/3,AB/106 (Item 106 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04352577 80236683 PMID: 6930702
DRB resistance in Chinese hamster and human cells: genetic and biochemical characteristics of the selection system.
Gupta RS; Siminovitch L
Somatic cell genetics (UNITED STATES) Mar **1980**, 6 (2) p151-69, ISSN 0098-0366 Journal Code: VAJ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Stable mutants resistant to the nucleoside **analog** 5,6-dichloro-1-beta-D-ribofuranosyl benzimidazole (DRB), which interferes with **RNA** synthesis, have been selected in Chinese hamster ovary (CHO) and human diploid fibroblasts. In CHO cells, upon treatment with the mutagen ethyl-methane sulfonate (EMS), a linear dose--response between the concentration of mutagen and the frequency of DrbR mutants was observed in the range of 20--300 micrograms/ml. The selection system did not show cell

density or cross-feeding effects, and the optimal expression time following mutagenesis was found to be 2--3 days for CHO cells and 5--6 days for human fibroblasts. The DrbR mutation behaved codominantly in DrbR x DrbS hybrids. Addition of DRB affected nucleoside uptake to a similar extent in both wild-type and mutant cells, indicating that the drug was able to enter the mutant cells. The failure of DrbR mutants to show any cross-resistance to other toxic nucleoside **analogs** examined suggests that the action of DRB does not involve the initial phosphorylation step. DRB addition did not cause any marked inhibition of either **RNA polymerase** I or **RNA polymerase** II activity from both wild-type and mutant cells in vitro, indicating that its effect on **RNA** synthesis may be indirect.

10/3,AB/107 (Item 107 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04064386 82247817 PMID: 6954467
Mechanism of action of dichloro-beta-D-ribofuranosylbenzimidazole: effect on in vitro transcription.
Zandomeni R; Mittleman B; Bunick D; Ackerman S; Weinmann R
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) May **1982**, 79 (10) p3167-70, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: AI-13231, AI, NIAID; CA-10815, CA, NCI; CA-21124, CA, NCI; +
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The adenosine **analog** 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole (DRB) and its mono- and triphosphate derivatives inhibit **RNA polymerase** II-specific transcription in an extract of whole HeLa cells. The **analog** does not inhibit **RNA polymerase** III-specific adenovirus VA **RNA** transcription in the whole cell extract. With purified **RNA polymerase** II under nonspecific transcription conditions, no effect on DRB could be detected. DRB is equally effective in inhibiting in vitro transcription from several of the adenovirus promoters and the human epsilon-globin gene. The inhibitory effects are in the order DRB greater than DRB monophosphate greater than DRB triphosphate. Thus DRB acts in vitro presumably on systems in which specific **RNA polymerase** II initiation of transcription occurs and with no detectable effect on premature termination. This will provide a suitable model for study of the molecular mechanism of action of DRB on transcription.

10/3,AB/108 (Item 108 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04060761 83103115 PMID: 7151173
Mechanism of **RNA polymerase** II--specific initiation of transcription in vitro: ATP requirement and uncapped runoff transcripts.
Bunick D; Zandomeni R; Ackerman S; Weinmann R
Cell (UNITED STATES) Jul **1982**, 29 (3) p877-86, ISSN 0092-8674 Journal Code: CQ4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The ATP **analog** 5'-adenylyl imidodiphosphate (AMP-PNP) inhibits transcription of specific genes by the **RNA polymerase** II contained in whole cell extracts, not only with promoters that contain A as the first nucleotide of the transcript, but also with those that initiate transcripts with G or U. The **analog** AMP-PNP (a competitive inhibitor of ATP) probably acts at the level of initiation of transcription, but it

can be used for elongation by **RNA polymerase** II in isolated nuclei or in the whole cell extract. AMP-PNP and the other imidotriphosphates have little effect on purified HeLa cell **RNA polymerase** II initiation and elongation of transcription. Since **RNA polymerase** III in the crude system both initiates and elongates transcripts with AMP-PNP, we conclude that the availability of the beta-gamma bond of ATP is an indispensable requirement for faithful and specific in vitro initiation only by **RNA polymerase** II in the whole cell extract. Uncapped U- or G-initiated transcripts were obtained in the presence of UMP-PNP or GMP-PNP, the respective imidodiphosphate **analogs** . The presence of the 5'-terminal imidotriphosphate at the same oligonucleotide as the cap for U-initiated precursors established that transcription initiation and capping occur at the same site. Capping is not required for transcription by **RNA polymerase** II in the in vitro system. Methylation of the 2' ribose of the initiating nucleotide does not occur on the imidonucleotide containing 5' ends of adenovirus EIV or murine leukemia virus long terminal repeat.

10/3,AB/109 (Item 109 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04056151 82245297 PMID: 7048064
Nucleotide **analogs** with modified sugar residue, in the **RNA** synthesis reaction of **RNA polymerase** from Escherichia coli]
Analogi nukleotidov, modifitsirovannye po sakharnomu ostatku, v reaktsii sinteza RNK RNK-polimerazoi iz Eshcherichia coli.
Aivazashvili VA; Bibilashvili RSh; Florent'ev VL
Molekuliarnaia biologiia (USSR) May-Jun **1982**, 16 (3) p493-8, ISSN 0026-8984 Journal Code: NGX
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
Influence of NTP **analogs** with the modified sugar residue on **RNA** synthesis catalyzed by E. coli **RNA polymerase** was studied. It was shown that **analog** with ribose residue substituted by hydrocarbon chain (-CH2-)2,3,4 as well as the **analogs** with opened ribose ring do not incorporate into the **RNA** chain. These compounds imped **RNA** elongation (Ki = 1.5--2.0 . 10(-3) M) due to their ability for reversible binding with the enzyme. These **analogs** inhibit the incorporation of all four natural NTP into **RNA** to the same extent, independently on the nature of the bases. In contrast, 3'-substituted **analogs** of NTP compete only with the homologous substrate for incorporation into **RNA**. The 3'-OMe-NTP incorporate into 3'-end of **RNA** and stop **RNA** propagation. The rate of 3'-OMe-NTP incorporation into **RNA** is 50--100 times lower, than that of the natural substrates.

10/3,AB/110 (Item 110 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04053492 82167340 PMID: 7068578
Mouse DNA **polymerase** accompanied by a novel **RNA polymerase** activity: purification and partial characterization.
Yagura T; Kozu T; Seno T
Journal of biochemistry (JAPAN) Feb **1982**, 91 (2) p607-18, ISSN 0021-924X Journal Code: HIF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A mouse DNA **polymerase** accompanied by a novel **RNA polymerase** activity and its specific protein factor (stimulating factor) were purified from Ehrlich ascites tumor cells and partially

characterized. The DNA **polymerase** was thought to be a subspecies of DNA **polymerase** alpha, and to be accompanied by or copurified with **RNA polymerase** activity capable of synthesizing **RNA**, which was probably utilized as a primer for subsequent DNA polymerization on a template of poly(dT) or poly(dC). This coupled reaction by **RNA** and DNA **polymerase** activities required the stimulating factor in addition to ribo- and deoxyribonucleotide substrates, although the degree of requirement depended on the kind of template and ribonucleotide substrate: the activity to incorporate dATP with poly(dT) plus ATP depended greatly on the stimulating factor, while the activity to incorporate dGTP with poly(dC) did not when GTP was added at high concentrations. GDP could be substituted for GTP, but the activity with poly(dC) plus GDP depended largely on the stimulating factor. Involvement of known **RNA polymerases** in the activity with poly(dT) was excluded, because addition of purified mouse **RNA polymerases** I and II had no effect on the incorporation of dATP, and alpha-amanitin (100 micrograms/ml) did not inhibit the incorporations of dATP and ATP. Analysis of the inhibition by the nucleotide **analog** 2',3'-dideoxynucleoside 5'-triphosphate (ddNTP) further supported the involvement of new **RNA polymerase** ; ddNTPs inhibited the activities with poly(dT) and poly(dC) significantly more than **RNA polymerases** I and II or DNA **polymerase** alpha activity with poly(dT) . oligo(rA) and poly(dC) . oligo(dG) as template. Lineweaver-Burk analysis of the inhibitions showed that ddATP inhibited competitively with respect to ATP, and ddGTP inhibited competitively with respect to GDP but noncompetitively with respect to GTP.

10/3,AB/111 (Item 111 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04027962 82075082 PMID: 6796536
Analogs of amanin. Synthesis of Ile3-amaninamide and its diastereoisomeric (S)-sulfoxide.
Zanotti G; Birr C; Wieland T
International journal of peptide and protein research (DENMARK) Aug **1981**, 18 (2) p162-8, ISSN 0367-8377 Journal Code: GSD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Ile3-amaninamide (3-R) and its diastereomeric sulfoxide (3-S) are obtained by oxidation of the bicyclic thioether peptide 2 by hydrogen peroxide in acetic acid. 2 was prepared by an intramolecular Savige-Fontana reaction of the linear octapeptide tert.-butylester 4 whose N-terminal Boc-Hpi residue on treatment with TFA loses the Boc group and reacts under thioether formation with the released cysteine-SH. The concomitantly deprotected carboxyl terminus is coupled intramolecularly with the free amino group of the secocompound 5 using the MA or DCCI method, thus forming the homodetic peptide ring. Compounds 3-R and 3-S agree very well with **analog** samples in chiroptical behavior. Thioether 2 and sulfoxide 3-R exert 50% inhibition of **RNA polymerase** II (or B) from Drosophila melanogaster in 10(-6) M solution whereas Ki of 3-S is about five times higher.

10/3,AB/112 (Item 112 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03490216 80101443 PMID: 118447
Distinctive nucleotide sequences of promoters recognized by **RNA polymerase** containing a phage-coded "sigma-like" protein.
Talkington C; Pero J
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Nov **1979**, 76 (11) p5465-9, ISSN 0027-8424 Journal Code: PV3

Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We report the nucleotide sequences of two promoters for bacteriophage SP01 "middle" genes. These promoters are recognized by a modified form of Bacillus subtilis **RNA polymerase** that contains a phage-coded "sigma-like" regulatory protein (gp28) in place of the bacterial sigma factor. Both promoters shared the identical hexanucleotide 5'A-G-G-A-G-A at about 35 base pairs preceding the start point of transcription and the identical heptanucleotide 5'-T-T-T-A-T-T-T (T is the thymine **analog** 5-hydroxymethyluracil in SP01 DNA) located about 10 base pairs preceding the transcriptional start point. The significance of these sequences in comparison with nucleotide sequences of promoters recognized by sigma-containing **RNA polymerases** is discussed.

10/3,AB/113 (Item 113 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03483305 80049864 PMID: 387781
Synthesis and properties of fluorescent nucleotide substrates for DNA-dependent **RNA polymerases**.
Yarbrough LR; Schlageck JG; Baughman M
Journal of biological chemistry (UNITED STATES) Dec 10 **1979**, 254 (23) p12069-73, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A new class of fluorescent nucleotide **analogs** which contain the fluorophore 1-aminonaphthalene-5-sulfonate attached via a gamma-phosphoamidate bond has been synthesized. Both the purine and pyrimidine **analogs** have fluorescence emission maxima at 460 nm. Cleavage of the alpha-beta-phosphoryl bond produces change in both the absorption and fluorescence emission spectra. The fluorescence of the pyrimidine **analogs** is quenched; cleavage of the alpha-beta-phosphoryl bond of the UTP **analog** produces about a 14-fold increase in fluorescence intensity at 500 nm. Under the same conditions the fluorescence of the CTP **analog** increases about 8-fold, whereas the fluorescence of the purine **analogs** shows only a slight change. These derivatives are good substrates for Escherichia coli **RNA polymerase** with only slightly increased Km values and with Vmax values about 50 to 70% that of the normal nucleotides. They are used less efficiently by wheat germ **RNA polymerase** II. The ATP **analog** can be used by E. coli **RNA polymerase** to initiate **RNA** chains.

10/3,AB/114 (Item 114 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03451496 77023780 PMID: 989743
Inhibition of mammalian polyadenylate **polymerase** by 2-aza-1,N6-etheno-adenosine triphosphate.
Keshgegian AA; Tsou KC; Furth JJ
Cancer research (UNITED STATES) Sep **1976**, 36 (9 pt.1) p3151-5, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
2-Aza-1,N6-etheno-adenosine triphosphate (aza-epsilonATP), a fluorescent **analog** of adenosine triphosphate, significantly inhibits polyadenylate [poly(A)] **polymerase** of bovine lymphosarcoma and calf thymus, with 50% inhibition at 200 muM (in the presence of an equal concentration of adenosine triphosphate). Calf thymus **RNA**

polymerases II and III are inhibited 32 and 20%, respectively, by a 3.8-fold excess of aza-epsilonATP; DNA **polymerase** alpha is not inhibited. The inhibition of poly(A) **polymerase** by aza-epsilonATP appears to be competitive with adenosine triphosphate; incorporation of aza-epsilonATP is not observed. Polymers of 2-aza 1,N6-etheno-adenosine monophosphate are used as primers, but pootly. 1,N-Etheno-adenosine triphosphate and 9-beta-D-arabinofuranosyladenine triphosphate are poor inhibitors of poly(A) **polymerase** ; adenosine diphosphate is ineffective. Deoxyadenosine triphosphate inhibits to the same extent as aza-epsilonATP, while other naturally occurring nucleotides inhibit poly(A) **polymerase** to varying degrees, with deoxynucleoside triphosphates more potent than ribonucleoside triphosphates. Inhibition of poly(A) **polymerase** by naturally occurring nucleoside triphosphates suggests that nucleotides may regulate the enzyme in vivo; inhibition by the fluorescent **analog** aza-epsilonATP suggests that this compound may be useful in elucidating poly(A) metabolism in both normal and neoplastic cells.

10/3,AB/115 (Item 115 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03447122 76167569 PMID: 131127
ATPase activity required for termination of transcription by the Escherichia coli protein factor rho.
Howard BH; de Crombrugghe B
Journal of biological chemistry (UNITED STATES) Apr 25 **1976**, 251 (8) p2520-4, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The relationship between the **RNA**-dependent beta-gamma ATPase in purified rho preparations and rho-mediated termination of transcription has been investigated. In a purified in vitro system, transcription from lambdagal DNA has been carried out using either ribonucleoside triphosphates (NTPs) or four ribonucleoside 5'-(beta-gamma-imino)triphospha tes (NMP-P(NH)Ps) as **RNA** precursors. In the presence of NTPs, rho termination activity results in (a) the synthesis of rho-dependent transcripts which are of discrete size by polyacrylamide gel analysis and (b) a marked reduction by hybridization assay in **RNA** transcribed distal to the rho-sensitive termination site tR. In the presence of four NMP-P(NH)Ps, which are not substrates for the beta-gamma ATPase, termination by rho is completely abolished, whereas rho-independent termination occurs normally. Addition of ATP to transcription reactions containing four NMP-P(NH)Ps restores termination, ruling out the possibility that the termination activity of rho is nonspecifically inhibited by the **analog** preparations. We interpret our data as strongly suggesting that the **RNA**-dependent beta-gamma ATPase activity of rho is required for rho-mediated termination of transcription.

10/3,AB/116 (Item 116 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03447029 76165279 PMID: 1261543
The interdependence of magnesium with spermidine and phosphoenolpyruvate in an enzyme-synthesizing system in vitro.
Fuchs E
European journal of biochemistry (GERMANY, WEST) Mar 16 **1976**, 63 (1) p15-22, ISSN 0014-2956 Journal Code: EMZ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The DNA-dependent syntheses of different enzymes of the bacteriophages T3

and T7 were studied in an Escherichia coli system in vitro with respect to the optimal Mg2+ concentration and its interdependence with substituting (e.g. spermidine) and complexing agents (e.g. phosphoenolpyruvate). The following results were obtained. 1. The optimal conditions for the syntheses of the different enzymes were not identical. The optima for **RNA polymerase** synthesis were 8 mM Mg2+, 10 mM P-pyruvate and 3 mM spermidine; for S-adenosyl-L-methionine cleaving enzyme synthesis, 6 mM Mg2+, 6 mM P-pyruvate and 3 mM spermidine; and for lysozyme synthesis, 13-18 mM Mg2+, 28 mM P-pyruvate and 3-0 mM spermidine. 2. The optimal conditions for the synthesis of **analog** enzymes (**RNA polymerases** and lysozymes) from the two templates were identical with experimental error. 3. Mg2+ and spermidine substituted for each other in relation to the number of their charges. 4. The apparent complexing of one Mg2+ molecule required the addition of 3-5 P pyruvate molecules. 5. Under the optimal conditions the enzyme-synthesizing activity was higher by more than a factor of 10 compared to previously described systems.

10/3,AB/117 (Item 117 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03442937 76073832 PMID: 1105009
Functional analysis of chemical systems in vivo using a logical circuit equivalent. V. Molecular biological interpretation of the self-reproducing automata theory and chemico-physical interpretation of information in biological systems.
Sugita M
Journal of theoretical biology (ENGLAND) Sep **1975**, 53 (1) p223-37, ISSN 0022-5193 Journal Code: K8N
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

10/3,AB/118 (Item 118 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03441886 76040378 PMID: 1101980
Effect of embichin (HN2) and its monofunctional **analog** (HN1) on chromatin and DNA matrix activity in an in vitro **RNA-polymerase** system]
Vliianie embikhina (HN2) i ego monofunktsional'nogo **analoga** (HN1) na matrichnuiu aktivnost' khromatina i DNK v RNK-polimeraznoi sisteme in vitro
Sokolov NA; Piker EG; Mironov NM; Tseitlin PI
Biulleten' eksperimental'noi biologii i meditsiny (USSR) Aug **1975**, 80 (8) p106-9, ISSN 0365-9615 Journal Code: A74
Languages: RUSSIAN
Document type: Journal Article
Record type: Completed
Embichin inhibited the matrix activity of chromatin and DNA in the **RNA-polymerase** system in vitro much more than its monofunctional **analogue**. Chromatin possessed a greater sensitivity to the action of embichin in comparison with the deproteinised DNA. However, with the action of a monofunctional embichin **analogue** there was a greater reduction of the matrix activity of DNA in comparison with chromatin. The depression mechanism of the matrix activity of chromatin with the action of embichin was apparently associated with the capacity of the latter to form the DNA-protein bonds in the chromatin composition.

10/3,AB/119 (Item 119 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03435846 75095652 PMID: 1112826
Purification and characterization of bacteriophage gh-I-induced deoxyribonucleic acid-dependent ribonucleic acid **polymerase** from Pseudomonas putida.
Towle HC; Jolly JF; Boezi JA
Journal of biological chemistry (UNITED STATES) Mar 10 **1975**, 250 (5) p1723-33, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Infection of Pseudomonas putida by the bacteriophage gh-L-induced the synthesis of a novel DNA-dependent **RNA polymerase** . This gh-L-induced **RNA polymerase** was purified to near homogeneity. It was shown to be distinct from the host **RNA polymerase** (alpha-2 beta beta sigma) physically and in respect to many of its catalytic properties. The gh-L-induced **RNA polymerase** was composed of a single polypeptide of approximately 98,000 molecular weight. The divalent metal ion requirement for in vitro **RNA** synthesis by the gh-L-**polymerase** could be satisified with Mg-2+, but not with Mn-2+. **Rna** synthesis by the gh-L **polymerase** was highly resistant to inhibition by rifampicin and streptolydigin but could be inhibited by relatively low concentrations of KCl or the rifamycin derivative AF/013. The structural **analog** of ATP, 3'-deoxyadenosine 5'-triphosphate, inhibited both the gh-L-induced and the host **RNA polymerases** by competing for a single binding site with ATP. The phage **polymerase** was extremely sensitive to this inhibitor, exhibiting an apparent K-i value (2 times 10-8 M) approximately 100 times lower than that for the host **RNA polymerase**. The gh-L **polymerase** had a highly specific template requirement for DNA from the homologous gh-L phage. It would not efficiently utilize denatured DNA templates and had only low levels of activity with pyrimidine-containing polydeoxyribonucleotide homopolymers.

10/3,AB/120 (Item 120 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02777583 79179784 PMID: 375193
2'-Deoxy-2'-fluorouridine-5'-triphosphates: a possible substrate for E. coli **RNA polymerase**.
Pinto D; Sarocchi-Landousy MT; Guschlbauer W
Nucleic acids research (ENGLAND) Mar **1979**, 6 (3) p1041-8, ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
dUflTP was tested as substrate in the E. coli **RNA polymerase** system using poly(dAT) as template. dUflTP could replace UTP when Mn++ was utilized as divalent cation instead of Mg++. The level of transcription with the fluoro **analog** was then 55% of that with UTP.

10/3,AB/121 (Item 121 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02769926 78218144 PMID: 353045
Transcription of T7 DNA containing modified nucleotides by bacteriophage T7 specific **RNA polymerase**.
Stahl SJ; Chamberlin MJ
Journal of biological chemistry (UNITED STATES) Jul 25 **1978**, 253 (14) p4951-9, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The interaction of bacteriophage T7 specific **RNA polymerase**

with its cognate promoter sites has been probed by selectively replacing bases in one T7 promoter site with base **analogs**. Base **analogs** such as 2,6-diaminopurine or hypoxanthine, which alter residues appearing in the minor groove of the DNA helix, prevent utilization of the promoter by T7 **RNA polymerase**. These **analogs** do not affect transcription which starts outside of the modified region. In contrast, base **analogs** that have alterations that appear in the major groove of the DNA helix, such as uracil, 5-bromouracil, 5-methylcytosine, 5-hydroxymethylcytosine, and [5-HgSR]pyrimidines, do not prevent utilization of the promoter. The deoxyribonucleoside **analog** 5'-imino-5'-deoxythymidine, an alteration appearing in the deoxyribose-phosphodiester backbone of the DNA helix, does not prevent promoter recognition. Haemophilus aegyptius restriction endonuclease III, which cleaves DNA at the sequence 5'GGCC3', does not act at sites in which the guanine residues in one of the two DNA strands have been substituted with hypoxanthine. This implicates the guanine amino group in the minor groove of the DNA helix as a possible recognition point for this restriction endonuclease.

10/3,AB/122 (Item 122 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02769640 78211129 PMID: 352398
Effects of purine riboside on nucleic acid synthesis in ascites cells.
Bohr V
Biochimica et biophysica acta (NETHERLANDS) Jun 22 **1978**, 519 (1) p125-37, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Purine riboside (nebularine, 9-beta-ribofuranosylpurine) is a naturally occurring base **analog** which closely resembles adenosine. It inhibits carcinogenic growth. Purine riboside strongly inhibits **RNA** and DNA synthesis in different cancer ascites cells. Gel electrophoretic analysis of **RNA** synthesis in vivo in the presence of purine riboside shows the ribosomal components to be inhibited the most. A method for assaying purine riboside or its phosphates intracellularly has been devised, and by using this it has been shown that purine riboside is extensively phosphorylated in the cells. The triphosphate derivative of purine riboside has been isolated and tested in the Escherichia coli **RNA polymerase** assay. It appears not to be incorporated into this type of **RNA** and to competitively inhibit this reaction with regard to ATP.

10/3,AB/123 (Item 123 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02768837 78186709 PMID: 656102
Synthesis and properties of a new fluorescent **analog** of ATP: adenosine-5'-triphosphoro-gamma-1-(5-sulfonic acid) napthylamidate.
Yarbrough LR
Biochemical and biophysical research communications (UNITED STATES) Mar 15 **1978**, 81 (1) p35-41, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

10/3,AB/124 (Item 124 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02768078 78157763 PMID: 347401
Template specific inhibitors of E. coli **RNA polymerase**.

Chou HJ; Froehlich JP; Pitha J
Nucleic acids research (ENGLAND) Mar **1978**, 5 (3) p691-6,
ISSN 0305-1048 Journal Code: O8L
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Electroneutral **analogs** of polynucleotides, poly-9-vinyladenine and poly-1-vinyluracil inhibit E. coli **RNA polymerase** in all combinations where the single stranded polynucleotides are used as templates and the vinyl **analogs** are complementary to them. As templates both the ribo- and deoxyribopolynucleotides were tested; variation of the template concentration in the presence of vinyl **analogs** produced a competitive pattern of inhibition. The electroneutral **analogs** do not inhibit the enzyme activity when non-complementary single stranded polynucleotides or double stranded polynucleotides are used as templates; the latter fully supports transcription even when one of the strands is complementary to the **analog**.

10/3,AB/125 (Item 125 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02557273 80043064 PMID: 497205
Differential effects of cordycepin triphosphate and 9 beta-D-arabinofuranosyladenine triphosphate on tRNA and 5 S **RNA** synthesis in isolated nuclei.
Leonard TB; Jacob ST
Biochimica et biophysica acta (NETHERLANDS) Jun 20 **1979**, 563 (1) p150-4, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Although cordycepin 5'-triphosphate (3'-dATP), at low concentrations, preferentially inhibits chromatin-associated poly(A) synthesis in isolated nuclei, higher levels of the inhibitor prevent both rRNA (**RNA polymerase** I activity) and hnRNA (**RNA polymerase** II activity) synthesis in vitro (Rose, K.M., Bell, L.E. and Jacob, S.T. (1977) Nature 267, 178-180). The present studies demonstrate that this nucleotide can also inhibit tRNA and 5 S **RNA** synthesis (**RNA polymerase** III activity). At 50-200 microgram/ml, 3'-dATP inhibits incorporation of [3H]UTP into tRNA and 5 S **RNA** by approximately 65%, whereas the syntheses of these RNAs were completely blocked when [3H]GTP was used as the substrate. These data suggest the formation of poly(U) in the tRNA and 5 S **RNA** regions, which is resistant to 3'-dATP. In contrast, another ATP **analog** , Ara-ATP, which selectively inhibits poly(A) synthesis, does not block tRNA and 5 S **RNA** synthesis in isolated nuclei. The production of these **RNA** species in isolated nuclei is also insensitive to Ara-CTP and 2'-dATP. These data suggest that 3'-dATP exerts general inhibitory effects on **RNA** synthesis and further substantiate the conclusion that Ara-ATP is a selective inhibitor of the polyadenylation reaction in vitro.

10/3,AB/126 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12082461 BIOSIS NO.: 199900377310
3-D organization of ribosomal transcription units after DRB inhibition of **RNA polymerase** II transcription.
AUTHOR: Le Panse Sophie; Masson Claude; Heliot Laurent; Chassery Jean-Marc; Junera Henriette Roberte; Hernandez-Verdun Daniele(a)
AUTHOR ADDRESS: (a)Institut Jacques Monod, 2 place Jussieu, 75251, Paris

Cedex 05**France
JOURNAL: Journal of Cell Science 112 (13):p2145-2154 July, **1999**
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: In each bead of the nucleolar necklace, using adenosine **analog** DRB-treated PtK1 cells, we investigated the three components of rDNA transcription, i.e. the gene, transcription factor UBF and transcripts. In situ hybridization revealed the unraveling and 3-D dispersion of most of the rDNA coding sequences within the nucleus. The signals were small, of similar intensity and tandemly organized in the necklace. This observation is compatible with the fact that they might correspond to single gene units. Active transcription was visualized in these units, demonstrating that they were active functional units. Transcript labeling was not similar for each unit, contrary to UBF labeling. UBF and rRNA transcripts were only partially colocalized, as demonstrated by 3-D image analysis and quantification. As visualized by electron microscopy, the necklace was composed of a small fibrillar center partially surrounded by a dense fibrillar component. The 3-D arrangement of this individual unit in thenecklace, investigated both by confocal and electron microscopy in the same cells, showed that the individual beads were linked by a dense fibrillar component. The reversibility of this organization after removal of DRB indicated that the beads in the necklace are certainly the elementary functional domain of the nucleolus. In addition, these results lead us to suggest that the organization of a functional domain, presumably corresponding to a single gene, can be studied by in situ approaches.

1999

1999

10/3,AB/127 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11665940 BIOSIS NO.: 199800447671
Sequence analysis of a functional **polymerase** (L) gene of bovine respiratory syncytial virus: Determination of minimal trans-acting requirements for **RNA** replication.
AUTHOR: Yunus Abdul S; Collins Peter L; Samal Siba K(a)
AUTHOR ADDRESS: (a)Virginia-Maryland Regional Coll. Veterinary Med., Univ. Maryland, College Park, MD 20742**USA
JOURNAL: Journal of General Virology 79 (9):p2231-2238 Sept., **1998**
ISSN: 0022-1317
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The complete nucleotide sequence of a functional clone of the large **polymerase** (L) gene of bovine respiratory syncytial virus (BRSV) strain A51908 was determined by analysis of cloned cDNAs obtained from genomic and mRNAs. The BRSV L gene is 6573 nt in length and the derived polypeptide has 2162 aa. Alignment of the sequences of the BRSV L gene, and its encoded protein, with sequences of the L gene and protein of human respiratory syncytial virus strain A2 showed 77% identity at the nucleotide level and 84% identity at the amino acid level. By comparison, the L gene and protein of avian pneumovirus showed only 50% identity at the nucleotide level and 64% identity at the amino acid level. A minigenome was constructed to encode a BRSV vRNA **analogue** containing the gene for chloramphenicol acetyltransferase (CAT) under the control of putative BRSV transcription motifs and flanked by the BRSV

genomic termini. Transfection of plasmids encoding the BRSV minigenome, nucleocapsid protein (N), phosphoprotein (P) and L protein, each under the control of T7 promoter, into cells infected with a vaccinia virus recombinant expressing the T7 **RNA polymerase** gave rise to CAT activity and progeny with the minigenome. This result indicates that the N, P and L proteins are necessary and sufficient for transcription and replication of the BRSV minigenome and are functional. Further, inclusion of small amounts of the M2 protein along with the N, P and L proteins greatly augmented minigenome transcription.

1998

10/3,AB/128 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11490021 BIOSIS NO.: 199800271353
Synthesis and **RNA polymerase** incorporation of the degenerate ribonucleotide **analogue** rPTP.
AUTHOR: Moriyama K; Negishi K; Briggs M S J; Smith C L; Hill F; Churcher M J; Brown D M; Loakes D(a)
AUTHOR ADDRESS: (a)Med. Res. Council, Centre Protein Engineering, Hills Road, Cambrdige CB2 2QH**UK
JOURNAL: Nucleic Acids Research 26 (9):p2105-2111 May 1, **1998**
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The synthesis and enzymatic incorporation into **RNA** of the hydrogen bond degenerate nucleoside **analogue** 6-(beta-D-ribofuranosyl)-3,4-dihydro-8H-pyrimido(4,5-c)(1,2)oxazin-7-one (P) is described. The 5'-triphosphate of this **analogue** is readily incorporated by T3, T7 and SP6 **RNA polymerases** into **RNA** transcripts, being best incorporated in place of UTP, but also in place of CTP. When all the uridine residues in an HIV-1 TAR **RNA** transcript are replaced by P the transcript has similar characteristics to the wild-type TAR **RNA**, as demonstrated by similar melting temperatures and CD spectra. The P-substituted TAR transcript binds to the Tat peptide ADP-1 with only 4-fold lowered efficiency compared with wild-type TAR.

1998

10/3,AB/129 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11430114 BIOSIS NO.: 199800211446
Interplay between positive and negative elongation factors: Drawing a new view of DRB.
AUTHOR: Yamaguchi Yuki; Wada Tadashi; Handa Hiroshi(à)
AUTHOR ADDRESS: (a)Dep. Biomolecular Eng., Fac. Biosci. Biotechnol., Tokyo Inst. Technol., 4259 Nagatsuta-cho, Mido**Japan
JOURNAL: Genes To Cells 3 (1):p9-15 Jan., **1998**
ISSN: 1356-9597
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: DRB is a classic inhibitor of transcription by **RNA polymerase** II (pol II). Although it has been demonstrated that DRB

inhibits the elongation step of transcription, its mode of action has been elusive. DRB also markedly inhibits human immunodeficiency virus (HIV) transcription, by targeting the elongation which is enhanced by the HIV-encoded transactivator Tat. Two factors essential for DRB action have recently been identified. These factors, positive transcription elongation factor b (P-TEFb) and DRB sensitivity-inducing factor (DSIF), positively and negatively regulate pol II elongation, and are likely to be relevant to the function of Tat. In this review, we summarize the recent findings on these factors, and discuss a possible model for the molecular mechanism of DRB action.

1998

10/3,AB/130 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10926307 BIOSIS NO.: 199799547452
Enzyme-catalysed transformations of compounds containing the -CH-2-AsO-3H-2 group.
AUTHOR: Dixon Henry B F(a); Mutenda Esther K; Sparkes Michael J(a)
AUTHOR ADDRESS: (a)Dep. Biochemistry, Univ. Cambridge, Tennis Court Rd., Cambridge CB2 1QW**UK
JOURNAL: Applied Organometallic Chemistry 11 (4):p251-255 **1997**
ISSN: 0268-2605
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Enzymes that act on substrates R-O-PO-3H-2 often work on substrate **analogues** R-OAsO-3H-2; such substrates are unstable, since esters of H-3AsO-4 hydrolyse easily. They also form easily, so that an enzyme that acts on RO-PO-3H-2 often acts on a mixture of R-OH and arsenate via an ester that forms at the active site. Similarly coenzyme **analogues** may be formed; for example, a stable and active aspartate aminotransferase forms from the apoenzyme with free pyridoxal and arsenate. Enzymes that convert R-O-PO-3H-2 into a diester often act on R-CH-2-AsO-3H-2, a stable substrate **analogue**; then the product is unstable and hydrolyses to re-form the **analogue**, giving a futile cycle. For example, **RNA polymerase** acquires exonuclease activity in the presence of H-2O-3P-CH-2-AsO-3H-2; adenylate kinase acquires ATPase activity in the presence of the arsonomethyl **analogue** of AMP. A recent observation is that HO-CH-2CHOH-CH-2-CH-2-AsO-3H-2 is a good substrate for glycerol-3-phosphate dehydrogenase. The product is unstable and eliminates arsenite, sharing this ability with other 3-oxoalkylarsonates. Thus this enzyme-catalysed oxidation is a lethal synthesis, in view of the toxicity of arsenite. Another unusual biochemical reaction of an arsonic acid is seen in the ability of a bacterium to use arsonoacetate as its sole source of carbon and energy. In contrast with the elimination of arsenite by 3-oxoalylarsonic acids, 3-oxoalkylphosphonic acids, R-CO-CH-2-CH-2-PO-3H-2, are stable. 2-Oxoalkylphosphonic acids, R-CO-CH-2-PO-3H-2, however, are moderately unstable to hydrolysis, yielding phosphate and R-CO-CH-3. 2-Oxoalkylarsonic acids, R-COCH-2-AsO-3H-2, decompose in the same way, but much more readily, yielding arsenate.

1997

10/3,AB/131 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10718591 BIOSIS NO.: 199799339736
Specific and nonspecific inhibition of transcription by DNA PNA, and phosphorothioate promoter **analog** duplexes.
AUTHOR: Hamilton Susan E; Iyer Mridula; Norton James C; Corey David R(a)
AUTHOR ADDRESS: (a)Howard Hughes Med. Inst., Dep. Pharmacology, Univ. Texas Southwestern Med. Cent. at Dallas, 5323**USA
JOURNAL: Bioorganic & Medicinal Chemistry Letters 6 (23):p2897-2900 **1996**
ISSN: 0960-894X
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: DNA duplexes **analogous** to the promoters for SP6 or T7 **RNA polymerase** inhibit transcription with exquisite selectivity. By contrast, phosphorothioate oligomers inhibit nonselectively, and peptide nucleic acid (PNA) duplexes and PNA:DNA heteroduplexes do not inhibit at all. The absence of recognition of proteins by PNAs may prove to be a substantial advantage for their use as anti-sense agents and nucleic acid probes.

1996

10/3,AB/132 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10630149 BIOSIS NO.: 199699251294
Physical and biological characteristics of the antitumor drug actinomycin D **analogues** derivatized at N-methyl-L-valine residues.
AUTHOR: Takusagawa Fusao(a); Wen Li; Chu Wenhua; Li Qifang; Takusagawa Ken T; Carlson Robert G; Weaver Robert F
AUTHOR ADDRESS: (a)Dep. Biochem., Univ. Kansas, Lawrence, KS 66045**USA
JOURNAL: Biochemistry 35 (40):p13240-13249 **1996**
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The crystal structure of the DNA-actinomycin D (AMD) complex and a simple molecular modeling study indicated that AMD **analogues** derivatized at N-methyl-L-valine residues (fifth amino acid residue in the cyclic depsipeptide of AMD) could bind to DNA as strongly as the parent AMD. The **analogues** in which N-methyl-L-valine residues were replaced with L- and D-forms of N-methylvalines, N-methylthreonines, N-methylphenylalanines, N-methyltyrosines, and N-methyl-O-methyltyrosines have been totally synthesized. The characteristics of binding of the **analogues** to various DNAs including DNA-1 (d(TATATATGCATATATA)), DNA-2 (d(TATATACGCGTATATA)), DNA-3 (d(ATATATAGCTATATAT)), and DNA-4 (d(ATATATGGCCATATAT)) have been examined by using visible absorption spectrum methods. The association constants calculated from the absorption spectra indicate that the modifications of the N-methyl-L-valine residues in the AMD molecule do affect the DNA binding characteristics of the **analogues**. The L-aromatic **analogues** bind slightly better than the L-aliphatic **analogues** except for binding to DNA-1 (-TGCA-), whereas the D-aliphatic **analogues** bind consistently better than the D-aromatic **analogues**. In the L-form **analogues**, the L-Tyr **analogue** has the highest overall association constant, whereas the D-Val **analogue** has the highest association constant among the D-form **analogues**. In spite of substitution of bulky aromatic groups, the D-aromatic **analogues** bind to the DNA-1 quite well. However, D-aromatic **analogues** have significantly reduced their binding capacities to the other DNAs, indicating that the substitution of the D-aromatic residues creates a

unique four-base sequence preference (-TGCA-). The **RNA polymerase** inhibitory activities of the AMD **analogues** in vivo have been examined using human cells (HeLa). All AMD **analogues** except for the L-Thr **analogues** severely inhibit **RNA** synthesis at relatively low drug concentrations. The D-Val, L-OMT, L-Phe, and D-Phe **analogues** inhibit **RNA** synthesis more strongly than the natural antibiotic (AMD itself).

1996

10/3,AB/133 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09778782 BIOSIS NO.: 199598233700
Total chemical synthesis of a ribozyme derived from a group I intron.
AUTHOR: Whoriskey Susan K; Usman Nassim; Szostak Jack W(a)
AUTHOR ADDRESS: (a)Dep. Mol. Biol., Massachusetts General Hosp., Boston, MA 02114**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 92 (7):p2465-2469 **1995**
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We describe the complete chemical synthesis of a ribozyme that catalyzes template-directed oligonucleotide ligation. The specific activity of the synthetic ribozyme is nearly identical to that of the same enzyme generated by in vitro transcription with T7 **RNA polymerase**. The ribozyme is derived from a group I intron and consists of three **RNA** fragments of 36, 43, and 59 nt that self-assemble to form a catalytically active complex. We have site-specifically substituted ribonucleotide **analogs** into this enzyme and have identified two 2'-hydroxyl groups that are required for full catalytic activity. In contrast, neither the 2'-hydroxyl nor the exocyclic amino group of the conserved guanosine in the guanosine binding site is necessary for catalysis. By allowing the ribozyme to be modified as easily as it; substrates, this synthetic ribozyme system should be useful for testing specific hypotheses concerning ribozyme-substrate interactions and tertiary interactions within the ribozyme.

1995

10/3,AB/134 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09509486 BIOSIS NO.: 199497517856
Correction of BA 94089054. Proximity between nucleotide/dinucleotide and metal ion binding sites in DNA-dependent **RNA polymerase** from Escherichia coli. Addition of author name and address, and correction of address from Dep. Med., Div. Cardiol., Univ. Missouri, Columbia, MO 65212, USA. Erratum published in BIOCHEMISTRY Vol. 33. Iss. 30. 1994. p. 9032.
AUTHOR: Tyagi Suresh C(a); Wu Felicia Y-H
AUTHOR ADDRESS: (a)Dep. Biochem. Cell Biol., State Univ. N.Y. Stony Brook, Stony Brook, NY 11794-5215**USA
JOURNAL: Biochemistry 31 (28):p6447-6453 **1992**
ISSN: 0006-2960
DOCUMENT TYPE: Article; Erratum
RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: In order to understand translocation in transcription, it is important to develop a continuous functional assay for **RNA polymerase** (RNAP) activity in vitro. Fluorescent derivatives of ATP, UTP, UpA, and CpA with aminonaphthalene-5-sulfonic acid (AMNS) attached to the nucleotide triphosphates via a gamma-phosphoramidate bond or to the dinucleotide monophosphates via a 5'-secondary amine linkage were synthesized (Tyagi, S. C., & Wu, F. Y.-H. (1987) J. Biol. Chem. 262, 10684-19688). The fluorescent emission spectra of (5'-AmNS)UpA, (5'-AmNS)CpA, (gamma-AmNS)ATP, and (gamma-AmNS)UTP overlap the absorption spectrum of co-substituted **RNA polymerase** (Co-RNAP) and ensure fluorescence resonance energy transfer (FRET) between the fluorescent **analog** and Co(II) in Co-RNAP. The binding constants at a single site for (gamma-AmNS)ATP, (gamma-AmNS)UTP, (5'-AmNS)UpA, and (5'-AmNS)CpA were observed to be 7.11, 5.26, 0.52, and 0.61 mu-M, respectively, in Co-RNAP and 5.70, 3.42, 0.12, and 0.21 mu-M, respectively, in Zn-RNAP. (8-AmTEMPO)ATP, with the spin probe AmTEMPO attached to the C-8 position at ATp (Tyagi, S. C. (1991) J. Biol. Chem. 266, 17936-17940), and Mn(3'-OCH-3)UTP were synthesized. Mn-I(II)-substituted **RNA polymerase** (Mn-RNAP) is prepared. The single site binding constants for (8-AmTEMPO)ATP and Mn(3'-OCH-3)UTP were 3.58 and 2.35 mu-M in Zn-RNAP and 5.77 and 3.43 mu-M in Mn-RNAP, respectively. These results indicate that dinucleotides bind much more tightly than mononucleotides in RNAP and that the binding constants are roughly the same for both Co- and Zn-substituted RNAP. FRET distances were found to be 16.6, 16.8, 17.7, and 14.4 ANG between the binding sites for (gamma-AmNS)ATP, (gamma-AmNS)UTP, (5'-AmNS)UpA, and (5'-AmNS)CpA, respectively, and the Co(II) in the beta-subunit of RNAP. Steady-state kinetic measurements on the incorporation of these **analogs** into **RNA** indicate that binding between substrate and RNAP becomes looser in the presence of DNA and other components of **RNA** synthesis. This indicates that these **analogs** undergo some alteration during catalysis.

1992

10/3,AB/135 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09080459 BIOSIS NO.: 199497088829
Photocrosslinking analysis of protein-**RNA** interactions in E. coli transcription complexes.
AUTHOR: Hanna Michelle M
AUTHOR ADDRESS: Dep. Bot.-Microbiol., Univ. Okla., Norman, OK 73019**USA
JOURNAL: Cellular & Molecular Biology Research 39 (4):p393-399 **1993**
ISSN: 0968-8773
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Regulation of transcription involves numerous specific protein-nucleic acid interactions. We have utilized photochemical crosslinking to identify interactions between Escherichia coli transcription proteins and the nascent **RNA** in several transcription complexes, including initiation, elongation, and antitermination complexes. We have developed new nucleotide **analogs**, 5-APAS-UTP and 5-APAS-CTP, which are tagged with photocross-linking groups on base positions that do not interfere with normal Watson-Crick base-pairing. These **analogs** are incorporated at internal positions in **RNA** by E. coli **RNA polymerase** without disrupting **RNA** secondary structures. We have also used 8-azido-ATP, which can be

incorporated uniquely into the 3' end of the **RNA**, to analyze interactions at the enzyme active site. Interactions between the **RNA** and the **polymerase** subunits, and the effect of various transcription factors, including NusA, NusB, NusE, and NusG, have been examined in complexes containing RNAs from 4 to approximately 80 nucleotides. At almost every **RNA** position examined, both the beta and beta' subunits are contacted, but never the alpha subunit or NusA. An effect of NusA on the core labeling has been observed in some complexes, however. Sigma is contacted by nucleotides within three nucleotides of the +1 position on the DNA.

1993

10/3,AB/136 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09078093 BIOSIS NO.: 199497086463
Lack of synergy in the inhibition of HIV-1 reverse transcriptase by combinations of the 5'-triphosphates of various anti-HIV nucleoside **analogs**.
AUTHOR: White E Lucile(a); Parker William B; Ross Larry J; Shannon William M
AUTHOR ADDRESS: (a)Kettering-Meyer Lab., Southern Res. Inst., 2000 Ninth Ave. S., Birmingham, AL 35205**USA
JOURNAL: Antiviral Research 22 (4):p295-308 **1993**
ISSN: 0166-3542
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: 3'-Deoxy-3'-azidothymidine (AZT) has been shown to synergistically inhibit the replication of human immunodeficiency virus type 1 (HIV-1) in cell culture when combined with several other 2',3'-dideoxynucleoside **analogs**. In an effort to understand the biochemical mechanism of this synergy, we have examined the effect of combinations of the 5'-triphosphate of AZT (AZT-TP) with either ddCTP, ddATP, or the 5'-triphosphate of the carbocyclic **analog** of 2',3'-didehydro-2',3'-dideoxyguanosine (carbovir) on both the **RNA** -directed and DNA-directed DNA **polymerase** activity of HIV-1 reverse transcriptase. Kinetic studies, which evaluated the ability of these combinations to competitively inhibit the enzyme, showed that AZT-TP could not bind to the enzyme with either the **RNA** or DNA template at the same time as either of the other three inhibitors. None of these **analogs** could affect the incorporation of another **analog** into the DNA chain by the HIV-1 reverse transcriptase. These results indicated that synergistic inhibition of the HIV-1 reverse transcriptase is not responsible for the synergistic antiviral activity seen in cell culture with combinations of these nucleoside **analogs**.

1993

10/3,AB/137 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08989788 BIOSIS NO.: 199396141289
Effects of Bacillus intermedius RNAse on the reproduction of the yeast Candida tropicalis.
AUTHOR: Kupriyanov-Ashina F G; Kolpakov A I; Egorov S Yu
AUTHOR ADDRESS: Dep. Microbiol., Kazan State Univ., Kazan**Russia

JOURNAL: Biologicheskie Nauki (Moscow) 0 (4):p90-100 **1992**
ISSN: 0470-4606
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Russian; Non-English
SUMMARY LANGUAGE: Russian; English

ABSTRACT: The effect of Bacillus intermedius RNAse on the reproduction of Candida tropicalis and synthesis of the main biopolymers in the yeast cells. It has been found that stimulating action of the enzyme appears at the concentration of 10-5-10-6 mg/ml and does not depend on the physiological state of the sowing culture. The connection between the increase of the ionic penetration and stimulation of the **RNA** and proteins synthesis in the yeast cells subjected to the RNAse action is shown. The mechanism of chromatine-associated **RNA-polymerase** activation is suggested to include the alteration of the ionic penetration of cells under the RNAse action.

1992

10/3,AB/138 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08961078 BIOSIS NO.: 199396112579
Elements controlling follicular expression of the s36 chorion gene during Drosophila oogenesis.
AUTHOR: Tolias Peter P(a); Konsolaki Mary; Halfon Marc S; Stroumbakis Nikolaos D; Kafatos Fotis C
AUTHOR ADDRESS: (a)Public Heatlh Res. Inst., 455 First Ave., New York, NY 10016**USA
JOURNAL: Molecular and Cellular Biology 13 (9):p5898-5906 **1993**
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An 84-bp proximal regulatory region (PRR) of the Drosophila melanogaster s36 chorion gene is sufficient for directing proper temporal and spatial expression of a reporter gene in three domains of the follicle: anterior, posterior, and main body. Here we show that the fidelity of PRR-directed s36 expression is dependent on the proper dorsal-ventral differentiation of the follicular epithelium, which requires the Drosophila epidermal growth factor receptor homolog. Transgenic analysis of site-directed mutants of the PRR suggests that s36 expression is regulated by the concerted action of multiple positive activators. Several cis-acting transcriptional elements have been identified: some appear to function in a quantitative manner, while others either are essential or appear to regulate expression in particular spatial domains. The approximate locations of these regulatory elements have been defined; some map within sequences that are strongly conserved in widely divergent dipteran species. In fact, the PRR **analog** of the medfly Ceratitis capitata Ccs36 gene directs expression in a manner similar to the D. melanogaster s36 PRR. We propose a model for transcriptional regulation of s36 based on the prechoriogenic polarization of the follicular epithelium that surrounds the developing egg chamber.

1993

10/3,AB/139 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08923607 BIOSIS NO.: 199396075108
Bacteriophage T7 **RNA polymerase**: Fluorine-19 nuclear magnetic resonance observations at 5-fluorouracil-substituted promoter DNA and **RNA** transcript.
AUTHOR: Rastinejad Fraydoon; Lu Ponzy(a)
AUTHOR ADDRESS: (a)Dep. Chem., Univ. Pa., Philadelphia, PA 19104**USA
JOURNAL: Journal of Molecular Biology 232 (1):p105-122 **1993**
ISSN: 0022-2836
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have substituted 5-fluorodeoxyuridine (5-FdU) in place of thymidine in defined positions along synthetic bacteriophage T7 promoter DNA sequences. None of the fluoro-substitutions in the promoter DNA sequence reduced transcription yields with T7 **RNA polymerase** significantly. Substitutions on the coding template strand reduced transcription yields when placed at +3, but not at +4. 19F-n.m.r. spectra from transcription reactions and, gel analysis of transcription products show that T7 **RNA polymerase** correctly and efficiently utilizes 5-FUTP as a **RNA** substrate **analog**. The fluorine atom provides a sensitive probe for monitoring the local environment, base sequence and solvent exposure at the DNA major groove through its 19F-n.m.r. resonance. Buffer dependencies of the fluorine chemical shift and digestion patterns with DNase I suggest that the T7 promoter base-pairs near the transcription start site are distorted with a more open minor groove and less solvent accessible major groove. Previous chemical footprinting data of promoter-**polymerase** complexes yield a picture that T7 **RNA** minor groove features on the same side of DNA flanking both sides of this region. Consistent **polymerase** recognizes major groove features in the region from positions -7 to -11 and minor groove features on the same side of DNA flanking both sides of this region. Consistent with this, 19F-n.m.r. observations identify two additional positions, -8 and -17, involved in promoter recognition on this side of the DNA helix. On the other hand, our observations also implicate the opposite side of the DNA helix, primarily at positions -14 and -15, as major groove recognition sites for T7 **RNA polymerase**. In addition, n.m.r. spectra from 5-FdU-substituted base-pairs -2 and -3, suggest either additional interactions on the same side of the DNA helix as -14 and -15, or distortions in the DNA structure.

1993

10/3,AB/140 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08895185 BIOSIS NO.: 199396046686
Cicaprost, a prostacyclin **analog**, protects renal function in uninephrectomized dogs in the absence of changes in blood pressure.
AUTHOR: Villa Eduardo; Martinez Javier; Ruilope Luis M; Mampaso Francisco; Sancho Jose M; Robles Rafael G(a)
AUTHOR ADDRESS: (a)Servicio Endocrinologia, Hospital Ramon y Cajal, Carr. Colmenar Km 9, 1 28034 Madrid**Spain
JOURNAL: American Journal of Hypertension 6 (4):p253-257 **1993**
ISSN: 0895-7061
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Ten dogs presenting mild chronic renal failure and hypertension after 27 months of uninephrectomy, during which they received a high sodium and high protein diet, were divided in two groups (n = 5) and followed for 15 months. The same diet was maintained and one of the groups received cicaprost treatment. The animals were periodically tested for biochemical and clinical parameters, and at months 0, 3, 6, and 15, glomerular filtration rate and renal plasma flow (RPF) were measured. Renal biopsies were made after 6 months of follow-up. Control group showed a higher thickening of pre- and intraglomerular portions of arteriolar vessels and an enhancement of mesangial matrix when compared with the treated group. Cicaprost also induced a significant elevation in RPF and a significant decrease in filtration fraction. All these findings suggest that cicaprost, an oral stable prostaglandin I-2 **analog**, could have a protective renal effect in this experimental model.

1993

10/3,AB/141 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08887970 BIOSIS NO.: 199396039471
Synthesis and characterization of a new photocrosslinking CTP **analog** and its use in photoaffinity labeling Escherichia coli and T7 **RNA polymerases**.
AUTHOR: Hanna Michelle M; Zhang Yuying; Reidling Jack C(a); Thomas Matthew J; Jou Jerry
AUTHOR ADDRESS: (a)Dep. Biol. Chem., Univ. California, Irvine, CA**USA
JOURNAL: Nucleic Acids Research 21 (9):p2073-2079 **1993**
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A new photocrosslinking CTP **analog** that functioned as a substrate during transcription was synthesized and used to photoaffinity label E. coli and bacteriophage T7 **RNA polymerases**. This **analog**, 5-((4-azidophenacyl)thio) cytidine-5'-triphosphate (5-APAS-CTP) contains an aryl azide group approximately 10 ANG from the nucleotide base and specifically replaced CTP during synthesis of **RNA** by both **polymerases**. **Analog** was placed at the 3' end or internally within **RNA**. Both **polymerases** inefficiently incorporated two 5-AP AS-CMP molecules sequentially, as was found for the related 5-APAS-UMP. **Analog** was placed at the 3' end of **RNA** in transcription complexes paused at the site of Q-modification of E. coli **RNA polymerase**, downstream of the lambda PR' promoter (+ 16), a pause that requires specific DNA sequences but no apparent **RNA** hairpin. Crosslinking was examined in the presence and absence of the NusA protein, which enhances the transcriptional pause at this site and is required for Q modification of the **polymerase**. Crosslinking of the 3' end of the **RNA** to NusA was not observed, consistent with our earlier results involving a NusA-enhanced pause site downstream from an **RNA** hairpin.

1993

10/3,AB/142 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07999248 BIOSIS NO.: 000093054921
ON THE MECHANISM OF LOW CONCENTRATIONS OF ADAPTOGENES INFLUENCE UPON THE

FUNCTIONAL ACTIVITY OF NORMAL AND TRANSFORMED CELL ELEMENTS IN-VITRO
AUTHOR: UDINTSEV S N; SCHAKHOV V P; BOROVSKOI I G
AUTHOR ADDRESS: RES. INST. PHARMACOL., TOMSK SCI. CENT., ACAD. MED. SCI. USSR, TOMSK, USSR.
JOURNAL: BIOFIZIKA 36 (4). 1991. 624-627. **1991**
FULL JOURNAL NAME: Biofizika
CODEN: BIOFA
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: Influence of water solutions of chemically pure adaptogene - synthetic **analog** of Rhodiola rosea extract phenol composition (SAR) on functional activity of hemopoietic and tumor cells of mice with Ehrlich ascite cancer was studied in vitro. The periodical character of SAR effects was shown to be different for both types of cells, and at 1 .times. 10-2 and 1 .times. 10-26 M concentrations simultaneous stimulation of blood marrow cells colony-forming activity and inhibition of the latter in tumor elements was revealed. Essential changes of reactions of both cell types after adding the DNA-dependent **RNA polymerase** blocker actinomycin D permit to suggest SAR effects to be connected with drug influence on the membrane **RNA** of the target cells.

1991

10/3,AB/143 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07886793 BIOSIS NO.: 000092135786
E-1BF IS AN ESSENTIAL **RNA POLYMERASE** I TRANSCRIPTION FACTOR WITH AN INTRINSIC PROTEIN KINASE ACTIVITY THAT CAN MODULATE RIBOSOMAL **RNA** GENE TRANSCRIPTION
AUTHOR: ZHANG J; NIU H; JACOB S T
AUTHOR ADDRESS: DEP. PHARMACOL. MOL. BIOL., CHICAGO MED. SCH., NORTH CHICAGO, ILL. 60064.
JOURNAL: PROC NATL ACAD SCI U S A 88 (19). 1991. 8293-8296. **1991**
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We previously described the purification and characterization of E1BF, a rat rRNA gene core promoter-binding factor that consists of two polypeptides of 89 and 79 kDa. When this factor was incubated in the absence of any exogenous protein kinase under conditions optimal for protein phosphorylation, the 79-kDa polypeptide of E1bF was selectively phosphorylated. The labeled phosphate could be removed from the E1BF polypeptide by treatment with calf intestinal alkaline phosphatase or potato acid phosphatase. Elution of the protein from the E1BF-promoter complex formed in an electrophoretic mobility-shift assay followed by incubation of the concentrated eluent with [.gamma.-32P]ATP resulted in the selective labeling of the 79-kDa band. The E1BF-associated protein kinase did not phosphorylate casein or histone H1. Fraction DE-B, a preparation containing **RNA polymerase** I and all **polymerase** I transcription factors (including E1BF), lost **polymerase** I transcriptional activity when treated with phosphatase. The phosphatase-induced inactivation of **polymerase** I activity associated with fraction DE-B could be reversed by the addition of purified E1BF. Treatment of purified E1BF with heat, SDS, or an ATP affinity **analog** eliminated its capacity to reactive dephosphorylated fraction DE-B. These data demonstrate that (i)

polymerase I promoter-binding factor E1BF contains an intrinsic substrate-specific protein kinase and (ii) E1BF is an essential **polymerase** I transcription factor that can modulate rRNA gene transcription by protein phosphorylation. Further, these studies have provided a direct means to identify a protein kinase or any other enzyme that can interact with a specific DNA sequence.

1991

10/3,AB/144 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07235093 BIOSIS NO.: 000090014966
ACTIVE SITE LABELING OF ESCHERICHIA-COLI TRANSCRIPTION ELONGATION COMPLEXES WITH 5-4 AZIDOPHENACYLTHIO-UTP
AUTHOR: DISSINGER S; HANNA M M
AUTHOR ADDRESS: DEP. CHEM., CALIF. COLL. MED., UNIV. CALIF., IRVINE, CALIF. 92717.
JOURNAL: J BIOL CHEM 265 (13). 1990. 7662-7668. **1990**
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Escherichia coli **RNA polymerase** transcription elongation complexes have been prepared that contain a photo-cross-linking uridine **analog** at only the 3' end, or one or two nucleotides removed from the 3' end, in the nascent **RNA** chain. Additionally, complexes have been isolated in which the **analog** has been substituted for every UMP residue, at positions ranging from 20 to 140 nucleotides from the 3' end. The **RNA** has been photochemically cross-linked to the **RNA polymerase** to identify the subunits that form the binding site(s) for these regions in the nascent **RNA**. The photo-cross-linking nucleotide **analog** used for these studies was 5-((4-azidophenacyl)thio)uridine-5'-triphosphate (5-APAS-UMP), which acts as a 10-15 .ANG. probe. With 5-APAS-UMP positioned only at the 3' end of the **RNA**, or one or two nucleotides from the 3' end, only the .beta. subunit appeared to be contacted. When the **analog** was positioned throughout the **RNA**, both the .beta. and .beta.' subunits were contacted. No labeling of the .sigma. or .alpha. subunits was observed with any **RNA** length. In addition to placing this **analog** at specific positions in short RNAs, we have carried out transcription studies with 5-APAS-UTP to determine the optimal UTP to **analog** ratio for production of full length, photoreactive transcripts. Surprisingly, we found that when transcription complexes were stalled shortly after initiation, by deletion of one ribonucleoside triphosphate to synchronize transcription, changes in transcriptional pausing occurred downstream. These results suggest that events that occur early in transcription can affect the elongation and/or termination events that occur far downstream form the promoter. This effect occurred even with UTP but was greately enhanced by replacement of UTP with either this **analog** or 4-thio-UTP. By enhancing the normal transcriptional pausing event, these **analogs** can serve as probes of the conformational changes that may exist in paused transcription complexes.
1990

10/3,AB/145 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06991850 BIOSIS NO.: 000089093114

SUBSTRATE PROPERTIES OF C METHYLNUCLEOSIDE TRIPHOSPHATES IN **RNA** SYNTHESIS REACTION CATALYSED BY ESCHERICHIA-COLI **RNA-POLYMERASE**

AUTHOR: SAVOCHKINA L P; SVIRYAEVA T V; BEIGEL'MAN L N; PADYUKOVA N SH; KUZNETSOV D A; LYSOV YU P; MIKHAILOV S N; BIBILASHVILI P SH
AUTHOR ADDRESS: ALL-UNION CARDIOL. SCI. CENT., ACAD. MED. SCI. SSR, MOSCOW 121552, USSR.

JOURNAL: MOL BIOL (MOSC) 23 (6). 1989. 1700-1710. **1989**
FULL JOURNAL NAME: Molekulyarnaya Biologiya (Moscow)
CODEN: MOBIB
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: 2'-C-methyl substituted and phosphonate **analogs** of UTP were prepared and together with the synthesized earlier 3'-C-methyl-UTP were investigated in the **RNA** synthesis reaction catalysed by Escherichia coli **RNA-polymerase**. Substrate properties of UTP **analogs** were studied in the presence of all natural triphosphates, in the absence of UTP and under conditions of soil substrate reaction. It was shown that UTP(3'CH3) is incorporated into the **RNA** chain and terminates further **RNA** elongation. Another **analog** UTP(2'CH3) may substitute natural UPT in **RNA** synthesis, but the effectivity of its incorporation is diminished. Phosphonate **analog** UTP(5'CH2) is a pseudoterminator of **RNA** synthesis. The conformational analysis of 2'- and 3'C-methylnucleosides by force-field method of calculation was carried out in order to find energetically forbidden conformations of these **analogs** due to the collision of bulky methyl group and a heterocyclic base. An attempt was made to fix the conformation of the substrate during its enzymatic transformation.

1989

06747616 BIOSIS NO.: 000088057047

EFFECT OF CYTOKININ ON PROTEIN KINASE ACTIVITY ASSOCIATED WITH **RNA-POLYMERASE** IN LUPINE COTYLEDONS

AUTHOR: ZAYAKIN V V; HAM I YA; KULAEVA O N
AUTHOR ADDRESS: ALL-RUSS. RES. INST. LUPIN, BRYANSK, USSR.

JOURNAL: FIZIOL RAST (MOSC) 36 (1). 1989. 11-17. **1989**
FULL JOURNAL NAME: Fiziologiya Rastenii (Moscow)
CODEN: FZRSA
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: DNA-dependent **RNA-polymerase** was isolated and partially purified from etiolated cotyledons of 5-day-old yellow lupin (Lupinus luteus L.). At all purification steps the enzyme possessed an autokinase activity requiring no additional protein substrates. In in vivo experiments 6-benzylaminpurine (6-BAP), when added to isolated lupin cotyledons, stimulated phosphorylation of **RNA-polymerase** and proportionally raised its activity. In in vitro experiments 6-BAP, when added to isolated **RNA-polymerase**, stimulated the autokinase activity of **RNA-polymerase**, without affecting the **RNA-polymerase** activity of the enzyme. The protein kinase activity associated with the **RNA-polymerase** enzyme was independent of the presence of 3',5'-cAMP and was not enhanced by the inactive cytokinin **analog** 6-methylaminopurine. A possible physiological role of the phosphorylation of **RNA-polymerase** is discussed.

1989

10/3,AB/147 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06272999 BIOSIS NO.: 000086107182
EFFECT OF CYTOKININ AND OTHER PHYTOHORMONES ON PROTEIN KINASES ASSOCIATED WITH CHROMATIN AND **RNA-POLYMERASE** I IN BARLEY LEAVES
AUTHOR: SELIVANKINA S YU; ROMANKO E G; NOVIKOVA G V; MUROMTSEVA D G; KULAEVA O N
AUTHOR ADDRESS: K.A. TIMIRYAZEV INST. PLANT PHYSIOL., ACAD. SCI. USSR, MOSCOW, USSR.
JOURNAL: FIZIOL RAST (MOSC) 35 (2). 1988. 266-274. **1988**
FULL JOURNAL NAME: Fiziologiya Rastenii (Moscow)
CODEN: FZRSA
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: Nuclear protein kinases were found in barley (Hordeum vulgare L.) leaves. The protein kinases associated with chromatin were activated with cytokinin both in vivo and in vitro. One of the protein kinases got isolated from chromatin together with **RNA-polymerase**-I, their activities correlating during leaf growth and upon kinetin action. Cytokinin activated the protein kinases on its application to the incubation medium. This activation followed the concentration pattern characteristic of the hormonal effects of cytokinins. The activation of protein kinases was revealed with natural (zeatin) and synthetic (kinetin and 6-benzylaminopurine) cytokinins but not with a cytokinin-inactive adenine **analog**. The chromatin protein kinases were also activated in vitro with abscisic acid and with auxin. The nuclear protein kinases are regarded as molecular targets for the action of cytokinins and other phytohormones, and their role in the mechanism of hormonal regulation of genetic apparatus in plants is discussed.

1988

10/3,AB/148 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06180527 BIOSIS NO.: 000086014709
FACTOR-DEPENDENT TRANSCRIPTION TERMINATION BY VACCINIA VIRUS **RNA POLYMERASE** EVIDENCE THAT THE CIS-ACTING TERMINATION SIGNAL IS IN NASCENT **RNA**
AUTHOR: SHUMAN S; MOSS B
AUTHOR ADDRESS: LAB. VIRAL DIS., NATL. INST. ALLERGY AND INFECTIOUS DIS., BETHESDA, MD. 20892.
JOURNAL: J BIOL CHEM 263 (13). 1988. 6220-6225. **1988**
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Transcription termination in vitro by vaccinia **RNA polymerase** is dependent on a trans-acting factor, VTF, that is associated with, if not identical to, the vaccinia mRNA capping enzyme. VTF-induced termination occurs approximately 50 nucleotides downstream of a signal sequence TTTTTNT in the non-transcribed templated strand; thus the cognate sequence UUUUUNU is expressed in the nascent **RNA**. To address the role of the nascent **RNA** in chain termination, the effects of nucleotide base **analog** substitutions were studied. Incorporation of bromo- (Br) UMP or iodo- (I) UMP into **RNA**

abrogated factor-dependent termination without preventing the synthesis of read-through transcripts. Substitution of either ITP or 7'-methylguanosine for GTP did not inhibit factor-dependent termination, nor did the substitution of BrCTP or ICTP for CTP. The early transcripts synthesized in vitro were sensitive to RNase T2 but resistant to RNase H, indicating an absence of extensive hybridization of **RNA** product to the DNA template. Substitution of BrUTP for UTP did not alter the nuclease sensitivity of the transcripts, suggesting that increased stability of **RNA**:DNA hybrid structures did not account for the **analog** effects. These results are consistent with a model in which recognition of the primary sequence UUUUUNU in nascen tRNA by the **polymerase** and/or VTF is required for transcription termination.

1988

10/3,AB/149 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06131028 BIOSIS NO.: 000085094180
CHARACTERIZATION OF A PHOTOAFFINITY **ANALOG** OF UTP 5 AZIDO-UTP FOR ANALYSIS OF THE SUBSTRATE BINDING SITE ON ESCHERICHIA-COLI **RNA POLYMERASE**
AUTHOR: WOODY A-Y M; EVANS R K; WOODY R W
AUTHOR ADDRESS: DEP. BIOCHEM., COLO. STATE UNIV., FORT COLLINS, COLO. 80523.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 150 (3). 1988. 917-924. **1988**
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The substrate binding site on E. coli **RNA polymerase** was investigated by photoaffinity labeling with a photoaffinity **analog** of UTP, 5-azido-UTP. We have established that 5-azido-UTP is a substrate for **RNA polymerase** by specific transcription on 229 bp DNA containing the gene II promoter of M13 phage. Analysis of the initial rate of **RNA** synthesis gives Km (5-azido-UTP) .apprx. 80 .mu.M. Photolabeling with varying concentrations of 5-azido-UTP follows a saturation curve with the midpoint occurring at a 5-azido-UTP concentrations of 65 .mu.M near to the Km obtained by kinetic analysis. 5-Azido-UTP photolabels the .beta.', .beta., and .sigma. subunits to about the same extent, both in the presence (33, 31, and 36%) and absence (35, 30 and 35%) of DNA. This labeling pattern is somewhat different from that obtained with 8-azido-ATP (.beta.' > .sigma. .mchgt. .beta. > .alpha.).

1988

10/3,AB/150 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06063220 BIOSIS NO.: 000085026369
UTILIZATION OF 5'-C METHYLNUCLEOSIDE TRIPHOSPHATES IN **RNA** SYNTHESIS REACTION CATALYZED BY ESCHERICHIA-COLI **RNA POLYMERASE**
AUTHOR: AIVAZASHVILI V A; MIKHAILOV S N; PADYUKOVA N SH; BIBILASHVILI R SH; KARPEISKII M YA
AUTHOR ADDRESS: ALL-UNION RES. INST. BIOTECHNOL., MOSCOW, USSR.
JOURNAL: MOL BIOL (MOSC) 21 (4). 1987. 1080-1091. **1987**
FULL JOURNAL NAME: Molekulyarnaya Biologiya (Moscow)
CODEN: MOBIB

RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: It was shown that **RNA-polymerase** is able to discriminate diasteroisomers of 5'-methyl-substituted **analogs** of ribonucleoside triphosphates (rNTP). Under conditions of soil substrate reactions when the **analog** is added to the presynthesized ternary complexes. D-allo- and L-talo-stereoisomers incorporate into **RNA** 100 and 1000 times, respectively, less effectively, then the natural rNTP. The effectives of incorporation of other 2'- and 3'-substituted **analogs** of rNTP were measured under the same conditions and compared with that of 5'-Me-rNTP. It was shown also that **RNA-polymerase** does not support long-chain **RNA** synthesis from 5'-Me-rNTP in the absence of natural rNTP. No more then two **analog** residues can be attached to the 3'-end of the presynthesized **RNA** under such conditions. Addition of one natural rNTP to this reaction mixture results in the synthesis of long alternating **RNA** containing D-allo-stereoisomer and natural rNTP residues. In the case of L-talo-stereoisomer **RNA** elongation is not inhibited, if the distance between the **analog** residues in the **RNA** chain is not shorter then five nucleotide residues. The rate of pyrophosphorolysis from the **RNA** of the **analogs** studied was the same as for the natural rNTP residues.

1987

10/3,AB/151 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06052321 BIOSIS NO.: 000085015470
KINETICS OF THE INHIBITION OF THE SYNTHESIS OF DINUCLEOTIDE PPPAPU CATALYZED BY ESCHERICHIA-COLI **RNA-POLYMERASE** ON PROMOTER A1 OF THE BACTERIOPHAGE T7 DELTA-DIII DNA BY 8 OXY-ATP UNDER CONDITIONS OF COUPLED SYNTHESIS OF DINUCLEOTIDE AND TRINUCLEOTIDE AND IN THE PRESENCE OF AN INCOMPLETE SET OF SUBSTRATES
AUTHOR: KURYAVYI V V; BRUSKOV V I
AUTHOR ADDRESS: INST. BIOL. PHYS., ACAD. SCI. USSR, PUSHCHINO, USSR.
JOURNAL: MOL BIOL (MOSC) 21 (2). 1987. 462-471. **1987**
FULL JOURNAL NAME: Molekulyarnaya Biologiya (Moscow)
CODEN: MOBIB
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: A kinetic analysis of inhibition of synthesis of dinucleotide pppApU catalyzed by Escherichia coli **RNA-polymerase** on A1 promoter of the DNA from T7 .DELTA. DIII phage mutant by 8-oxy-ATP under the conditions of the coupled synthesis of pppApU and pppApUpC and in the presence of an incomplete set of substrates, namely ATP, UTP, CTP, has been performed. It was found that 8-oxy-ATP is an unproductive **analog** of both ATP and CTP. A comparative analysis of the dissociation constants shows that 8-oxy-ATP binds at ATP center 3.3 times and at CTP center 540 times weaker than natural substrates. At the UTP center 8-oxy-ATP does not bind at all.

1987

10/3,AB/152 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05707631 BIOSIS NO.: 000084056037

SPECIFIC REQUIREMENT FOR ATP AT AN EARLY STEP OF IN-VITRO TRANSCRIPTION OF HUMAN MITOCHONDRIAL DNA
AUTHOR: NARASIMHAN N; ATTARDI G
AUTHOR ADDRESS: DIV. BIOL., INST. TECHNOL., PASADENA, CA 91125, USA.
JOURNAL: PROC NATL ACAD SCI U S A 84 (12). 1987. 4078-4082. **1987**
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The ATP concentrations allowing transcription of both heavy- and light-strand of human mtDNA in a HeLa cell mitochondrial lysate were found to cover a broad range, with a maximum around 2.5 mM, and with reproducible differences in the ATP responses curves for the transcription events. Direct measurements showed that nonspecific ATP degradation during the assay did not account for the high ATP requirement. 5'-Adenylyl imidodiphosphate (p[NH]ppA), an ATP **analog** with a nonhydrolyzable .beta.-.gamma. bond, was unable to substitute for ATP in supporting mtDNA transcription but greatly stimulated this transcription in the presence of a low concentration of exogenous ATP. Evidence was obtained indicating that p[NH]ppA did not support an early event in mtDNA transcription (formation of preinitiation complex or initiation), whereas this **analog** could substitute effectively for ATP in the subsequent elongation steps. These results pointed to a specific requirement for ATP at an early step of the transcription process.

1987

10/3,AB/153 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05627729 BIOSIS NO.: 000083100870
CHARACTERIZATION OF THE GUANOSINE 3'-DIPHOSPHATE 5'-DIPHOSPHATE BINDING SITE ON ESCHERICHIA-COLI **RNA** TO **POLYMERASE** USING A PHOTOPROBE 8 AZIDOGUANOSINE 3'-5'-BISPHOSPHATE
AUTHOR: OWENS J R; WOODY A-Y M; HALEY B E
AUTHOR ADDRESS: DEP. BIOCHEM., COLO. STATE UNIV., FT. COLLINS, COLO.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 142 (3). 1987. 964-971. **1987**
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Nucleotide binding sites on DNA-dependent **RNA** **polymerase** from E. coli have been studied by photoaffinity labeling with a GTP **analog** [.gamma.-32P]-8-AzidoGTP and a guanosine-3'-diphosphate-5'-diphosphate **analog**, 8-Azidoguanosine-3'-phosphate-5'-[5'-32P]phosphate. The guanosine diphosphate photoprobe labeled the .beta., .beta.', and .sigma. subunits with the .sigma. subunit being most heavily labeled. The GTP photoprobe also labeled the .beta., .beta.', .sigma. subunits but the .beta.' subunit was most heavily labeled. In competition experiments guanosine-3'-diphosphate-5'-[5'-32P]phosphate better than GTP, while the opposite was true for photolabeling with [.gamma.-32P]8-AzidoGTP. The guanosine diphosphate photoprobe inhibited transcription on E. coli DNA with Ki of ca. 150 .mu.M. Present studies suggest a unique ppGpp binding site distinct from substrate binding site(s) and this photoprobe may be used to localize this binding site(s).

1987

10/3,AB/154 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05270935 BIOSIS NO.: 000082111560
RAPID ENRICHMENT OF HELA TRANSCRIPTION FACTOR-IIIB AND FACTOR-VIIIC BY USING AFFINITY CHROMATOGRAPHY BASED ON AVIDIN-BIOTIN INTERACTIONS
AUTHOR: KASHER M S; PINTEL D; WARD D C
AUTHOR ADDRESS: DEP. BIOPHYS. AND BIOCHEM., YALE UNIV. SCH. MED., NEW HAVEN, CONN. 06510.
JOURNAL: MOL CELL BIOL 6 (9). 1986. 3117-3127. **1986**
FULL JOURNAL NAME: Molecular and Cellular Biology
CODEN: MCEBD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Plasmid DNA containing the adenovirus type 2 genes for VA **RNA** was linearized at a site distal to the gene, end labeled with a biotin-nucleotide **analog** of TTP, and incubated with avidin to form an avidin-biotinylated DNA complex. HeLa cell S100 extracts containing crude **RNA polymerase** III and transcription factors (TFs) IIIB and IIIC were programmed with the avidin-biotin-VA DNA to allow stable complex formation (A. B. Lassar, P. L. Martin, and R. G. Roeder, Science 222:740-748, 1983). Chromatography of the programmed extract over a biotin-cellulose affinity resin resulted in the selective, and virtually quantitative, retention of one of two stable preinitiation complexes, either VA-IIIC or VA-IIIC-IIIB, depending on the length of template incubation in the S100 extract. After washing the resin with 0.10 M and 0.25 M KCl to remove **RNA polymerase** III and nonspecifically bound proteins, respectively, TFIIIC was eluted from the VA-IIIC complex by the addition of 1.5 M KCl. The VA-IIIC-IIIB complex exhibited a higher salt stability. Most of TFIIIB and some TFIIIC were released by the addition of 1.5 M KCl; however, the majority of TFIIIC activity was recovered only after a subsequent 3.0 M KCl elution. The specific activity of the TFIIIC in the 3.0 M KCl fraction was 770-fold higher than that in the S100 extract, while the protein content of the 1.5 and 3.0 M KCl fractions was reduced 7,500- and 100,000-fold, respectively.

1986

10/3,AB/155 (Item 30 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05179551 BIOSIS NO.: 000082020172
SYNTHETIC AMATOXIN **ANALOGUE** A TWO-DIMENSIONAL PROTON NMR STUDY OF S DEOXY-3-ISOLEUCINE-7-D-ALANINE AMANITINAMIDE
AUTHOR: ZANOTTI G; D'AURIA G; PAOLILLO L; TRIVELLONE E
AUTHOR ADDRESS: DEP. CHEM., UNIV. NAPLES, NAPLES, ITALY.
JOURNAL: BIOCHIM BIOPHYS ACTA 870 (3). 1986. 454-462. **1986**
FULL JOURNAL NAME: Biochimica et Biophysica Acta
CODEN: BBACA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of substitution of L and D amino acids in amatoxin **analogues** is discussed in this paper. The structure of the **analog** where D-alanine substitutes for glycine in position 7 has been worked out in solution by two-dimensional NMR methods using a 500 MHz instrument. The combined use of COSY and NOESY two-dimensional spectra allows a clear assignment of the resonances. The use of the

coupling constants permits the calculation of the .rho. angles of the backbone. The NOE effects reveal the through-space contacts between protons of different peptide units, thus determining the rigidity of the amatoxin structure. On these grounds it has been possible to elucidate the conformation of the amatoxin **analogue** that resembles very closely that of .beta.-amanitin, thus explaining the high inhibitory activity toward **RNA polymerase** B.

1986

10/3,AB/156 (Item 31 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05084519 BIOSIS NO.: 000081042643
KINETICS OF INTERACTION OF METHYLENEDIPHOSPHONIC-ACID AND INORGANIC PYROPHOSPHATE WITH DNA-DEPENDENT **RNA POLYMERASE** II FROM CALF THYMUS
AUTHOR: FOMOVSKAYA G N; KOMISSARENKO S V
AUTHOR ADDRESS: A.V. PALLADIN INST. BIOCHEM., ACAD. SCI. UKR. SSR, KIEV, USSR.
JOURNAL: BIOKHIMIYA 50 (5). 1985. 839-843. **1985**
FULL JOURNAL NAME: Biokhimiya
CODEN: BIOHA
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: The kinetics of interaction of PPi and its diphosphonic **analog**, methylenediphosphonic acid (MDPA), with nucleoside triphosphates, DNA and Mg2+ binding sites of DNA-dependent **RNA polymerase** II from calf thymus was investigated. The values of apparent Km in the NTP polymerization reaction for ATP and CTP equal to 2.7 .cntdot. 10-4 and 1.8 .cntdot. 10-4 M, respectively, were determined. It was shown that MDPA and PPi competitively inhibited the **RNA polymerase** reaction with respect to nucleoside triphosphate. The inhbition constants (Ki) of ATP and CTP incorporation for MDPA were 2.2 8. 10-4 and 3.3 .cntdot. 10-4, respectively, while those of the nucleoside triphosphate incorporation for PPi were equal to 1.4 .cntdot. 10-4 and 2.0 .cntdot. 10-4 M, respectively. MDPA and PPi were incompetitive inhibitors of template (DNA) and Mn2+. A possible mechanism of inhibition of the **RNA polymerase** reaction by MDPA is proposed.

1985

10/3,AB/157 (Item 32 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04740920 BIOSIS NO.: 000080044047
ZINC DEFICIENCY AND THE EUGLENA-GRACILIS CHROMATIN FORMATION OF AN ALPHA AMANITIN-RESISTANT **RNA POLYMERASE** II
AUTHOR: FALCHUK K H; MAZUS B; BER E; ULPINO-LOBB L; VALLEE B L
AUTHOR ADDRESS: CENTER BIOCHEMICAL AND BIOPHYSICAL SCIENCES AND MEDICINE, HARV. MED. SCH., BOSTON, MASS. 02115.
JOURNAL: BIOCHEMISTRY 24 (10). 1985. 2576-2580. **1985**
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Both the single DNA-dependent **RNA polymerase** found in

Zn-deficient (-Zn) Euglena gracilis and the **RNA polymerase** III from Zn-sufficient (+Zn) cells were isolated by methods previously used to purify **polymerases** I and II. Like class II **polymerases**, the enzyme from -Zn organisms elutes from DNA-cellulose and phosphocellulose with 0.6 M NaCl and 0.35 M NH4Cl, respectively. It is inhibited by 8-hydroxyquinoline, 8-hydroxyquinoline-5-sulfonic acid, .alpha.,.alpha.'-bipyridyl, dipicolinic acid and 1,10-phenanthroline (OP); 4,7-phenanthroline, the nonchelating **analog**, does not inhibit. The pKI(OP) of this enzyme is identical with that of **polymerase** II but distinct from those of **polymerases** I and III. Elemental analysis confirms that Zn is the functional metal while Cu, Mn, Fe and Mg are absent. The -Zn enzyme is at least 4 orders of magnitude more resistant to .alpha.-amanitin (.alpha.-A) than the class II **polymerase**. Its response to .alpha.-A is unlike that of either **polymerase** I or **polymerase** III. Thus, -Zn cells contain a single, .alpha.-amanitin-resistant (.alpha.-Ar) **RNA polymerase**, whose behavior otherwise resembles that of the .alpha.-A-sensitive **polymerase** II.

1985

10/3,AB/158 (Item 33 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04627128 BIOSIS NO.: 000079040165
CAPPED MESSENGER **RNA** SPECIES MAY STIMULATE THE INFLUENZA VIRION **POLYMERASE** BY ALLOSTERIC MODULATION
AUTHOR: PENN C R; MAHY B W J
AUTHOR ADDRESS: DIV. VIROL., DEP. PATHOL., UNIV. CAMBRIDGE, LAB. BLOCK, ADDENBROOKE'S HOSP., HILLS ROAD, CAMBRIDGE, U.K.
JOURNAL: VIRUS RES 1 (1). 1984. 1-14. **1984**
FULL JOURNAL NAME: Virus Research
CODEN: VIRED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: **Analogs** of the mRNA 5'-terminal methyl cap structure were found to stimulate the influenza virion **RNA**-dependent **RNA polymerase**. The single nucleotide **analog** in m7GMP was incorporated into **RNA** during transcription in vitro, and the stimulatory effect was not additive with the primer ApG, suggesting that m7GMP stimulates the virion **polymerase** by priming virus-specific mRNA synthesis, as has been shown for ApG. Stimulation by m7G(5')ppp(5')m6Am2-O was additive with that by ApG, and it was not possible to demonstrate incorporation of the similar **analog** m7G(5')ppp(5')Am2-O into **RNA** during transcription. Evidently, these dinucleotide cap **analogs** stimulate the virion **polymerase** by allosteric modulation, independent of priming. This stimulation can be abolished by mutation, without loss of other activities associated with the cap-dependent endonuclease.

1984

10/3,AB/159 (Item 34 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04603215 BIOSIS NO.: 000079016252
PHOTOAFFINITY LABELING OF DNA-DEPENDENT **RNA POLYMERASE** FROM ESCHERICHIA-COLI WITH 8 AZIDO ATP
AUTHOR: WOODY A-Y M; VADER C R; WOODY R W; HALEY B E

AUTHOR ADDRESS: DEP. BIOCHEM., COLO. STATE UNIV., FORT COLLINS, CO 80523, USA.
JOURNAL: BIOCHEMISTRY 23 (13). 1984. 2843-2848. **1984**
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A photoaffinity **analog** of ATP, 8-azidoadenosine 5'-triphosphate (8-N3ATP), was used to elucidate the role of the various subunits involved in forming the active site of E. coli DNA-dependent **RNA polymerase**. 8-N3ATP was a competitive inhibitor of the enzyme with respect to the incorporation of ATP with Ki = 42 .mu.M; UTP incorporation was not affected. UV irradiation of the reaction mixture containing **RNA polymerase** and [.gamma.-32P]-8-N3ATP induced covalent incorporation of radioactive label into the enzyme. Analysis by gel filtration and nitrocellulose filter binding indicated specific binding. Subunit analysis by sodium dodecyl sulfate and sodium tetradecyl sulfate gel electrophoresis and autoradiography of the labeled enzyme showed that the major incorporation of radioactive label was in .beta.' and .sigma., with minor incorporation in .beta. and .alpha.. The same pattern was observed in the presence and absence of poly[d(A-T)] and poly[d(A-T)] plus ApU. Incorporation of radioactive label in all bands was significantly reduced by 100-150 .mu.M ATP; 100-200 .mu.M UTP did not show a noticeable effect. These results indicate major involvement of the .beta.' and .sigma. subunits in the active site of **RNA polymerase**. The observation of a small extent of labeling of the .beta. and .alpha. subunits, which was prevented by saturating levels of ATP, suggests that these subunits are in close proximity to the catalytic site.

1984

10/3,AB/160 (Item 35 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04599786 BIOSIS NO.: 000079012823
GENE IDENTIFICATION IN POLYTENE CHROMOSOMES SOME BALBIANI RING 2 GENE SEQUENCES ARE LOCATED IN AN INTERBAND-LIKE REGION OF CHIRONOMUS-TENTANS
AUTHOR: SASS H
AUTHOR ADDRESS: DEP. BIOCHEM. MOLECULAR BIOL., HARVARD UNIV., 7 DIVINITY AVENUE, CAMBRIDGE, MASS. 02138, USA.
JOURNAL: CHROMOSOMA (BERL) 90 (1). 1984. 20-25. **1984**
FULL JOURNAL NAME: CHROMOSOMA (Berlin)
CODEN: CHROA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Injection of C. tentans larvae with the nucleoside **analog** DRB (5,6-dichloro-1.beta.-D-ribofuranosylbenzimidazole) led to a drastic reduction of **RNA** synthesis in the polytene salivary gland chromosomes, accompanied by a dissociation of **RNA polymerase** B (or II) from the chromosomal template. The DRB injection also led to a recondensation of the Balbiani ring 2 (BR2) puff and the formation of a well-defined banding pattern at the site of previous puffing. In the recondensed condition in situ hybridization of cloned BR2 DNA demonstrated that BR2 gene sequences are located in a region that light microscopically appears to be an interband between bands IV-3B9 and IV-3B10. No hybridization exists over bands IV-3B8 and IV-3B10. The in situ hybridization over interband IV-3B9/10 differs from the result of previous hybridization of BR2 **RNA** to polytene chromosomes from Malpighian tubules of C. tentans that showed that the BR2 gene is located

in band IV-3B10. Due to the different hybridization probes used by the investigators both results are compatible with the location of the BR2 gene in a band-interband structure. Evidently, the repressed BR2 gene consists of 2 segments with different chromatin conformation (1 with relatively extended interband chromatin and 1 with condensed band chromatin), and the transcriptional and regulatory unit of the BR2 gene may extend from the interband into the band or vice versa.

1984

10/3,AB/161 (Item 36 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04599751 BIOSIS NO.: 000079012788
DRUG-INDUCED DISPERSAL OF TRANSCRIBED RIBOSOMAL **RNA** GENES AND TRANSCRIPTIONAL PRODUCTS IMMUNOLOCALIZATION AND SILVER STAINING OF DIFFERENT NUCLEOLAR COMPONENTS IN RAT CELLS TREATED WITH 5 6 DICHLORO-BETA-D-RIBOFURANOSYLBENZIMIDAZOLE
AUTHOR: SCHEER U; HUEGLE B; HAZAN R; ROSE K M
AUTHOR ADDRESS: DIVISION OF MEMBRANE BIOLOGY AND BIOCHEMISTRY, INSTITUTE OF CELL AND TUMOR BIOLOGY, GERMAN CANCER RESEARCH CENTER, D-6900 HEIDELBERG, FEDERAL REPUBLIC OF GERMANY.
JOURNAL: J CELL BIOL 99 (2). 1984. 672-679. **1984**
FULL JOURNAL NAME: Journal of Cell Biology
CODEN: JCLBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Upon incubation of cultured rat cells with the adenosine **analog** 5,6-dichloro-1-.beta.-D-ribofuranosylbenzimidazole (DRB), nucleoli reversibly dissociate into their substructures, disperse throughout the nuclear interior, and form nucleolar necklaces. This experimental system, which does not inhibit transcription of the rRNA genes, used immunocytochemistry to study the distribution of active rRNA genes and their transcriptional products during nucleolar dispersal and recovery to normal morphology. Antibodies to **RNA polymerase** I allow detection of template-engaged **polymerase**, and monoclonal antibodies to a ribosome protein (S1) of the small ribosomal subunit permit localization of nucleolar preribosome particles. Under the action of DRB transcribed rRNA, genes spread throughout the nucleoplasm and finally appear in the form of several rows, each containing several (up to 30) granules positive for **RNA polymerase** I and argyrophilic proteins. Nucleolar material containing preribosomal particles also appears in granular structures spread over the nucleoplasm but its distribution is distinct from that of rRNA gene-containing granules. Although transcriptional units and preribosomal particles are both redistributed in response to DRB, these entities retain their individuality as functionally defined subunits. Each **RNA polymerase**-positive granular unit represents a single transcription unit and each continuous array of granules (string of nucleolar beads) reflects the linear distribution of rRNA genes along a nucleolar organizer region. Based on the total number of **polymerase** I-positive granules, a minimum of 60 rRNA genes are estimated to be active during interphase of DRB-treated rat cells.

1984

10/3,AB/162 (Item 37 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04595832 BIOSIS NO.: 000079008869
CRYSTAL AND MOLECULAR STRUCTURE OF S DEOXO-3-ISOLEUCINEAMANINAMIDE A SYNTHETIC **ANALOG** OF AMANITA TOXINS
AUTHOR: SHOHAM G; REES D C; LIPSCOMB W N; ZANOTTI G; WIELAND T
AUTHOR ADDRESS: GIBBS LAB., DEP. CHEM., HARVARD UNIV., CAMBRIDGE, MA 02138.
JOURNAL: J AM CHEM SOC 106 (16). 1984. 4606-4615. **1984**
FULL JOURNAL NAME: Journal of the American Chemical Society
CODEN: JACSA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The crystal structure of S-deoxo[Ile3]amaninamide, a nontoxic synthetic derivative of the Amanita phalloides mushroom toxins (amatoxins), was determined by single-crystal X-ray diffraction. Six intramolecular H-bonds hold the bicyclic octapeptide in a compact conformation, which is very similar to the conformation of the naturally occurring (and toxic) amatoxin, .beta.-amanitin. The 30-fold reduction in binding affinity to **RNA polymerase** B of the title amatoxin, and probably of most of the other amatoxin **analogs** with altered side chain 3, is probably not due to alteration of backbone conformation. The 3 water molecules and 2 ethanol molecules, crystallized with the amatoxin, form a strong and extensive intermolecular H-bonding system.

1984

10/3,AB/163 (Item 38 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04362042 BIOSIS NO.: 000078091587
SYNTHESIS OF HUMAN U-1 **RNA** 2. IDENTIFICATION OF 2 REGIONS OF THE PROMOTER ESSENTIAL FOR TRANSCRIPTION INITIATION AT POSITION PLUS 1
AUTHOR: SKUZESKI J M; LUND E; MURPHY J T; STEINBERG T H; BURGESS R R; DAHLBERGG J E
AUTHOR ADDRESS: DEP. PHYSIOLOGICAL CHEMISTRY, UNIV. WISCONSIN-MADISON, MADISON, WI 53706.
JOURNAL: J BIOL CHEM 259 (13). 1984. 8345-8352. **1984**
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The requirements for human U1 **RNA** transcription catalyzed by **RNA polymerase** II were analyzed. In Xenopus laevis oocytes, a human U1 **RNA** gene with only 231 and 35 nucleotides of the 5' and 3' flanking regions, respectively, is able to support accumulation of human U1 **RNA**. The point in the template corresponding to the 5' end of U1 **RNA** is a site of transcription initiation. That result rules out the possibility that the 5' end of U1 **RNA** is generated by cleavage and capping of a precursor **RNA**. The accumulation of correctly initiated human U1 **RNA** transcripts requires at least 2 essential upstream elements. The region between positions -231 and -203 is indispensable for transcription both in oocytes and in vitro. The other region, between positions -105 and -6, fixes the location of the 5' ends of the U1 **RNA** transcripts in oocytes while not altering the overall level of transcription. This latter region contains a sequence located around position -50, which may serve as the **analog** of the T-A-T-A sequence in U1 and U2 **RNA** genes.

1984

10/3,AB/164 (Item 39 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04327177 BIOSIS NO.: 000078056720
NUCLEOSIDE 5'-BETA GAMMA PER OXY TRI PHOSPHATES
AUTHOR: GIBSON K J; LEONARD N J
AUTHOR ADDRESS: ROGER ADAMS LAB., SCH. CHEM. SCI., UNIV. ILL., URBANA, ILL. 61801.
JOURNAL: BIOCHEMISTRY 23 (1). 1984. 78-85. **1984**
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Procedures for the synthesis, purification and characterization of .beta.,.gamma.-peroxy **analogs** of the 8 common ribo- and deoxyribonucleoside triphosphates were developed. Although adenosine 5'-(.beta.,.gamma.-peroxytriphosphate) was stable to conditions in most biochemical systems, incubation of a solution of the **analog** at 100.degree. C led to formation of AMP and ATP, as well as ADP. NAD pyrophosphorylase [pig liver, EC 2.7.7.1] was the only enzyme among 13 tested for which adenosine 5'-(.beta.,.gamma.-peroxytriphosphate) was a good substrate, but the **analog** was an effective inhibitor for a number of kinases. The peroxy compounds tested inactive with Escherichia coli **RNA polymerase** [EC 2.7.7.6] and DNA **polymerase** I [EC 2.7.7.7], as well as with wheat germ **RNA polymerase** II.

1984

10/3,AB/165 (Item 40 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04321475 BIOSIS NO.: 000078051018
PACKING OF A SPECIFIC GENE INTO HIGHER ORDER STRUCTURES FOLLOWING REPRESSION OF **RNA** SYNTHESIS
AUTHOR: ANDERSSON K; BJORKROTH B; DANEHOLT B
AUTHOR ADDRESS: DEP. MED. CELL GENETICS, MED. NOBEL INSTITUTE, KAROLINSKA INSTITUTET, S-10401 STOCKHOLM 60, SWEDEN.
JOURNAL: J CELL BIOL 98 (4). 1984. 1296-1303. **1984**
FULL JOURNAL NAME: Journal of Cell Biology
CODEN: JCLBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Transcription of the Balbiani ring (BR) genes of the dipteran Chironomus tentans was inhibited by the nucleoside **analog** DRB (5,6-dichloro-1-.beta.-D-ribofuranosyl benzimidazole). The BR genes were emptied of **RNA polymerases** and the subsequent packing of the genes was monitored by transmission electron microscopy. The thin chromatin axis of the transcriptionally active genes condensed into a thick (20-25 nm) chromatin fiber, which was recorded as a linear structure, an open loop or a supercoiled loop. The compacted genes were finally packed into dense clumps of chromatin. Upon repression of **RNA** synthesis the BR gene template may attain the following consecutive stages with increasing compaction: transcription loop .fwdarw. linear thick fiber .fwdarw. open thick fiber loop .fwdarw. supercoiled thick fiber loop .fwdarw. dense chromatin. Within the chromatin blocks structures that resembled the supercoiled loops were discerned, suggesting that the final packing of the template might be accomplished by a close alignment of supercoiled loops.

1984

10/3,AB/166 (Item 41 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04273789 BIOSIS NO.: 000078003331
TOPOLOGICAL LINKAGE OF CIRCULAR DNA MOLECULES PROMOTED BY USTILAGO-MAYDIS REC-1 PROTEIN AND TOPO ISOMERASE
AUTHOR: KMIEC E B; KROEGER P E; BROUGHAM M J; HOLLOMAN W K
AUTHOR ADDRESS: DEP. IMMUNOL. MED. MICROBIOL., UNIV. FLA. COLL. MED., GAINESVILLE, FL 32610.
JOURNAL: CELL 34 (3). 1983. 919-930. **1983**
FULL JOURNAL NAME: Cell
CODEN: CELLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The formation of linked circular DNA molecules promoted by the combined action of rec1 protein and type I topoisomerase of U. maydis was studied. When ATP was added as cofactor to reactions containing rec1 protein, pairs of homologous circular DNA molecules became linked after addition of topoisomerase. Closed circular duplex molecules could be joined at homologous sites with circular single-stranded molecules or with other circular duplex molecules, provided that homologous single-stranded DNA fragments or **RNA polymerase** and nucleoside triphosphates were also added. Complexes formed were topologically linked through regions of heteroduplex DNA. When the **analog** adenylyl-imidodiphosphate was substituted for ATP, non-homologous pairs of circular DNA molecules became linked.

1983

10/3,AB/167 (Item 42 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04248963 BIOSIS NO.: 000077075008
SELECTIVE TRANSCRIPTION OF A CLONED CAULIFLOWER MOSAIC VIRUS DNA FRAGMENT IN-VITRO BY SOYBEAN **RNA POLYMERASE** II EC-2.7.7.6 IN THE PRESENCE OF DI NUCLEOTIDE PRIMERS
AUTHOR: COOKE R M; PENON P; GOT C; MIASSOD R
AUTHOR ADDRESS: LABORATOIRE DE PHYSIOLOGIE VEGETALE, EQUIPE DE RECHERCHE ASSOCIEE NO. 226, UNIVERSITE DE PERPIGNAN, AVENUE VILLENEUVE, F-66025 PERPIGNAN-CEDEX, FRANCE.
JOURNAL: EUR J BIOCHEM 137 (1-2). 1983. 365-372. **1983**
FULL JOURNAL NAME: European Journal of Biochemistry
CODEN: EJBCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Transcription of a cloned cauliflower mosaic virus (CaMV) DNA fragment (plasmid pCa8) was studied at a low enzyme:DNA ratio. Preincubation with purine nucleoside triphosphates leads to essentially random transcription medium certain combinations prime preferential transcription of the eukaryotic moiety of the chimeric plasmid. Characterization of transcription primed by the most efficient combination, ApG + ATP, shows that a low enzyme:DNA ratio is absolutely essential for selective initiation. The presence of the eukaryotic insertion is essential for the transcription of vector sequences. Analysis of **RNA** primed by ApG + ATP and of short chains synthesised in the presence of the GTP **analog** 3-OMeGTP shows a high degree of

selectivity of transcription initiation sites. Hybridization of primed **RNA** to restriction fragments of pCa8 shows that initiation occurs within a limited region of the inserted CaMV fragment.

1983

10/3,AB/168 (Item 43 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04201966 BIOSIS NO.: 000077028010
A FACTOR IN SEA-URCHIN EGGS INHIBITS TRANSCRIPTION IN ISOLATED NUCLEI BY SEA-URCHIN **RNA POLYMERASE** III
AUTHOR: MORRIS G F; MARZLUFF W F
AUTHOR ADDRESS: DEP. OF CHEMISTRY, FLA. STATE UNIV., TALLAHASSEE, FLA. 32306.
JOURNAL: BIOCHEMISTRY 22 (3). 1983. 645-653. **1983**
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Isolated nuclei from sea urchin [Lytechinus variegatus and Strongylocentrotus purpuratus] embryos synthesize **RNA** at a rate comparable to other animal cell nuclei. All 3 **RNA polymerases** are active as judged by .alpha.-amanitin sensitivity and hybridization to specific cloned DNA. Extracts were prepared from sea urchin eggs and embryos by extraction with 0.35 M KCl. None of the crude extracts had a large effect on total **RNA** synthesis. Extracts from sea urchin eggs inhibited **RNA polymerase** III activity in nuclei from blastula and gastrula embryos. There was no effect on the synthesis of rRNA by **RNA polymerase** I or on the synthesis of 2 **RNA polymerase** II products, histone mRNA and the sea urchin **analog** of U1 **RNA**. The inhibitor is present in 2 different species of sea urchin and was .apprx. 50-fold purified by DEAE cellulose and hydroxylapatite chromatography. The inhibitor is not present in extracts prepared from sea urchin blastula embryos.

1983

10/3,AB/169 (Item 44 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03993745 BIOSIS NO.: 000076079311
NO CORRELATION BETWEEN BINDING OF GLUCO CORTICO STEROIDS TO SPECIFIC CYTOPLASMIC PROTEINS IN-VIVO AND ENZYME INDUCTION IN THE RAT LIVER
AUTHOR: GROTE H; VOIGT J; SEKERIS C E
AUTHOR ADDRESS: INST. BOT., UNIV. HAMBURG, OHNHORSTSTR. 18, D-2000 HAMBURG 52, FEDERAL REPUBLIC OF GER.
JOURNAL: BIOCHEM J 212 (2). 1983. 305-312. **1983**
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Time- and dose-dependence of the formation of the different cytoplasmic hormone-protein complexes were studied in the rat liver after administration in vivo of [3H]cortisol or [3H]dexamethasone and compared with the stimulation of **RNA polymerase** B and induction of tyrosine aminotransferase and tryptophan oxygenase. No correlation could be found between formation in vivo of any of the 5 cytoplasmic

hormone-protein complexes found and stimulation of **RNA polymerase** B activity or enzyme induction. After administration of [3H]cortisol, different metabolites of cortisol could be demonstrated in the isolated hormone-protein complexes. No time- or dose-dependence of the metabolite patterns could be observed after application of hormone doses that were in the range of the biologically active doses. After administration of [3H]dexamethasone, the same hormone-protein complexes were observed, which contained, however, the injected steroid instead of metabolites. The cytoplasmic binding components present in the rat liver are enzymes involved in the metabolism of the glucocorticosteroids and that dexamethasone binds to these enzymes as a substrate **analog**.

1983

10/3,AB/170 (Item 45 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03909697 BIOSIS NO.: 000075087770
RAPID REFORMATION OF THE THICK CHROMOSOME FIBER UPON COMPLETION OF **RNA** SYNTHESIS AT THE BALBIANI RING GENES IN CHIRONOMUS-TENTANS
AUTHOR: ANDERSSON K; MAHR R; BJORKORTH B; DANEHOLT B
AUTHOR ADDRESS: DEPARTMENT OF MEDICAL CELL GENETICS, MEDICAL NOBEL INSTITUTE, KAROLINSKA INSTITUTET, S-10401 STOCKHOLM 60, SWEDEN.
JOURNAL: CHROMOSOMA (BERL) 87 (1). 1982 (RECD. 1983). 33-48. **1982**
FULL JOURNAL NAME: CHROMOSOMA (Berlin)
CODEN: CHROA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The ultrastructure of the Balbiani ring [BR] genes in C. tentans was studied during treatment with the **RNA** synthesis inhibitor DRB (5,6-dichloro-1-.beta.-D-ribofuranosyl-benzimidazole). This nucleoside **analog** blocks transcription at or near the initiation site but does not interfere with the elongation and termination processes. In the ordinary active state the BR genes display a 5 nm chromosome fiber, carrying densely distributed, growing ribonucleoprotein particles. When the transcriptional activity declines, a 10 nm fiber can be observed between sparsely distributed **RNA polymerases**. After passage of the last **RNA polymerase** the 10 nm fiber can be seen as well as its gradual packing into a 25 nm thick fiber. The active chromosome fiber is rapidly packed into higher order structures when the fiber is not directly involved in transcription. The formation of the thick fiber does not require that the gene along its entire length is devoid of active **RNA polymerases**. The thick fiber can again be mobilized for transcription, since in reversion experiments the BR genes appear as ordinary active genes with an extended nucleofilament and densely packed nascent transcription products. The dynamic behavior of the chromosome fiber during transcription is discussed as well as the packing and unpacking of a gene into higher order structures.

1982

10/3,AB/171 (Item 46 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03893826 BIOSIS NO.: 000075071899
PROBES OF EUKARYOTIC DNA DEPENDENT **RNA POLYMERASE** II EC-2.7.7.6 1. BINDING OF 9-BETA-D ARABINOFURANOSYL-6-MERCAPTO PURINE TO THE ELONGATION SUBSITE
AUTHOR: CHO J M; KIMBALL A P

AUTHOR ADDRESS: DEPARTMENT OF BIOCHEMICAL AND BIOPHYSICAL SCIENCES,
UNIVERSITY OF HOUSTON, CENTRAL CAMPUS, HOUSTON, TEXAS 77004, USA.
JOURNAL: BIOCHEM PHARMACOL 31 (16). 1982. 2575-2582. **1982**
FULL JOURNAL NAME: Biochemical Pharmacology
CODEN: BCPCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: 9-.beta.-D-Arabinofuranosyl-6-mercaptopurine (ara-6-MP) was used to affinity-label wheat germ DNA-dependent **RNA polymerase** II (or B). This nucleoside **analog** was a competitive inhibitor with respect to [3H]UMP incorporation. Natural substrates protected the enzyme from inactivation by ara-6-MP when the enzyme was preincubated with excess concentrations of substrates, suggesting that the inhibitor binds at the elongation subsite. The inhibitor bound the catalytic center of the enzyme with a stoichiometry of 0.6:1. The SH reagent, dithiothreitol, reversed the inhibition by ara-6-MP, suggesting that the 6-thiol group of the inhibitor was interacting closely with an essential cysteine residue in the catalytic center of the enzyme. Chromatographic analysis of the pronase-digestion products of the **RNA polymerase** II-ara-6-MP complex also showed that ara-6-MP had bound a cysteine residue. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of the denatured [6-35S]ara-6-MP-labeled **RNA polymerase** II revealed that over 80% of the radioactivity was associated with the IIb subunit of the enzyme.

1982

10/3,AB/172 (Item 47 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03637724 BIOSIS NO.: 000074053301
INHIBITION OF A NOVEL SUBSPECIES OF DNA **POLYMERASE** ALPHA BY 2'
DEOXY-2'-AZIDO ATP
AUTHOR: YAGURA T; KOZU T; SENO T; NISHIJIMA Y; OHTSUKA E; IKEHARA M
AUTHOR ADDRESS: DEP. VIROL., IMMUNOL., SAITAMA CANCER CENT. RES. INST.,
INA-MACHI, KITAADACHI-GUN, SAITAMA 362, JAPAN.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 104 (4). 1982. 1189-1195. **1982**
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: DNA **polymerase** .alpha.1, a subspecies of DNA **polymerase** .alpha. of (mouse) Ehrlich ascites tumor cells, was associated with a novel **RNA polymerase** activity and used poly(dT) and single-stranded circular fd DNA as a template without added primer in the presence of ribonucleoside triphosphates and a specific stimulating factor. DNA synthesis in the above system was inhibited by the ATP **analog**, 2'-deoxy-2'-azidoATP more than the DNA synthesis with poly(dT) .cntdot. oligo(rA) by DNA **polymerase** .alpha.1 and **RNA** synthesis is by mouse **RNA polymerases** I and II. Kinetic analysis showed that the **analog** inhibited DNA **polymerase** .alpha.1 activity on poly(dT) competitively with respect to ATP, suggesting that the **analog** inhibited **RNA** synthesis by the associated **RNA polymerase** activity.

1982

10/3,AB/173 (Item 48 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03578257 BIOSIS NO.: 000073081338
EVALUATION OF CARBODINE THE CARBOXYLIC **ANALOG** OF CYTIDINE AND RELATED CARBO CYCLIC **ANALOGS** OF PYRIMIDINE NUCLEOSIDES FOR ANTI VIRAL ACTIVITY AGAINST HUMAN INFLUENZA TYPE A VIRUSES
AUTHOR: SHANNON W M; ARNETT G; WESTBROOK L; SHEALY Y F; O'DELL C A; BROCKMAN R W
AUTHOR ADDRESS: KETTERING-MEYER LAB., SOUTH. RES. INST., BIRMINGHAM, ALA. 35255.
JOURNAL: ANTIMICROB AGENTS CHEMOTHER 20 (6). 1981. 769-776. **1981**
FULL JOURNAL NAME: Antimicrobial Agents and Chemotherapy
CODEN: AMACC
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Carbodine, the carbocyclic **analog** of cytidine, was found to possess significant antiviral activity against influenza virus types A0/PR-8/34 and A2/Aichi/2/68 (Hong Kong) in vitro. The compound selectively inhibited PR-8 influenza virus-induced cytopathogenic effects in Madin-Darby canine kidney cells and inhibited Hong Kong influenza virus replication in primary rhesus monkey kidney cell cultures. The 50% minimum inhibitory concentration for inhibition of human influenza type A viruses by carbodine was .apprx. 2.6 .mu.g/ml (i.e., in the range of antiviral potency of ribavirin but less potent than amantadine hydrochloride in concomitant assays). The fact that carbodine is metabolized to carbodine triphosphate in mammalian cells makes interference with the viral **RNA**-dependent **RNA polymerase** reaction a likely possibility for its principal mode of action. The carbocyclic **analogs** of uridine (the deamination product of carbodine), 2'-deoxycytidine, 3'-deoxycytidine, N,N-dimethylcytidine, N-methylcytidine and some related carbocyclic **analogs** of pyrimidine nucleosides were inactive against PR-8 influenza virus in vitro. The combination of carbodine plus tetrahydrouridine was no more effective in vitro than carbodine alone, thus indirectly indicating that deamination of carbodine probably did not occur to a significant degree during the cell culture experiments. Although reproducibly active in vitro, carbodine did not exhibit any efficacy against lethal influenza virus infections in mice when administered by either the i.p. or intranasal routes up to dose-limiting toxic levels.

1981

10/3,AB/174 (Item 49 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03550363 BIOSIS NO.: 000073053444
CONSERVED NUCLEOTIDE SEQUENCES IN TEMPORALLY CONTROLLED BACTERIO PHAGE PROMOTERS
AUTHOR: LEE G; PERO J
AUTHOR ADDRESS: BIOL. LAB., HARV. UNIV., CAMBRIDGE, MASS. 02138, USA.
JOURNAL: J MOL BIOL 152 (2). 1981. 247-266. **1981**
FULL JOURNAL NAME: Journal of Molecular Biology
CODEN: JMOBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Gene expression at a middle time in the lytic cycle of Bacillus subtilis bacteriophage SP01 is controlled by the product of phage gene 28 (gp28). gp28 is a sigma-like regulatory protein that directs the bacterial core **RNA polymerase** to bind and initiate transcription from promoter sites for phage middle genes. The location,

orientation and nucleotide sequences of 5 promoters in a cluster of middle genes on the phage genome are reported. All 5 promoters shared highly conserved nucleotide sequences that were centered at .apprx. 35 and 10 base-pairs upstream from their start points of transcription. Based on these conserved sequences it is proposed that **RNA polymerase** containing gp28 recognizes the prototype sequence 5'T--T-AGGAGA--A-TT in the -35 promoter region and the sequence 5'TTT-TTT in the -10 region. (In SP01 DNA, T is the thymine **analog** 5-hydroxymethyluracil.) These prototype sequences differ strikingly from the corresponding conserved regions of SP01 early gene promoters which are recognized by the unmodified B. subtilis **RNA polymerase** and which are highly homologous to promoters for Escherichia coli **RNA polymerase**. Sigma factors (host sigma and gp28) may dictate the recognition of both the -35 and -10 regions of promoters.

1981

10/3,AB/175 (Item 50 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03518482 BIOSIS NO.: 000073021562
ANALOGS OF AMANIN SYNTHESIS OF 3 ISO LEUCINE AMANINAMIDE AND ITS DIA STEREO ISOMERIC S SULFOXIDE
AUTHOR: ZANOTTI G; BIRR C; WIELAND T
AUTHOR ADDRESS: MAX-PLANCK-ISNT. MED. FORSCH., JAHNSTR. 29, D-6900 HEIDELBERG, W. GER.
JOURNAL: INT J PEPT PROTEIN RES 18 (8). 1981. 162-168. **1981**
FULL JOURNAL NAME: International Journal of Peptide and Protein Research
CODEN: IJPPC
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Ile3-amaninamide (3-R) and its diastereomeric sulfoxide (3-S) were obtained by oxidation of the bicyclic thioether peptide 2 by H2O2 in acetic acid. The peptide 2 was prepared by an intramolecular Savige-Fontana reaction of the linear octapeptide tert-butylester 4 whose N-terminal Boc-Hpi residue on treatment with TFA [trifluoroacetic acid] lost the Boc group and reacted under thioether formation with the released Cys-SH. The concomitantly deprotected carboxyl terminus was coupled intramolecularly with the free amino group of the secocompound 5 using the MA [mixed anhydride] or DCCI [dicyclohexylcarbodiimide] method, forming the homodetic peptide ring. Compounds 3-R and 3-S agreed well with **analog** samples in chiroptical behavior. Thioether 2 and sulfoxide 3-R exerted 50% inhibition of **RNA polymerase** 2 (or B) from Drosophila melanogaster in 10-6 M solution; Ki of 3-S was .apprx. 5 times higher.

1981

10/3,AB/176 (Item 51 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03281378 BIOSIS NO.: 000072009481
ENHANCEMENT OF TRANSCRIPTION OF THE SV-40 GENOME IN MOUSE EMBRYO CELLS BY PRE TREATMENT WITH 5 IODO-2'-DEOXY URIDINE
AUTHOR: SUAREZ H G; LANGE M; CASSINGENA R
AUTHOR ADDRESS: INST. RECH. SCI. SUR LE CANCER, B.P. NO 8, 94800 VILLEJUIF, FR.
JOURNAL: J GEN VIROL 52 (1). 1981. 135-140. **1981**
FULL JOURNAL NAME: Journal of General Virology

CODEN: JGVIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Treatment of mouse embryo (ME) cells with 5-iodo-2'-deoxyuridine (IdUrd) before infection with SV40 virus enhances T-antigen (T-Ag) production as detected by immunofluorescence and complement fixation. Cellular DNA and **RNA** synthesis are inhibited in SV40- and mock-infected cells after IdUrd treatment. The **analog** pretreatment significantly increases the amount of radiolabeled nuclear and cytoplasmic SV40-specific **RNA** and the **RNA polymerase** activity of the viral transcriptional complexes of the Sarkosyl supernatants, suggesting that the enhancement of SV40 T-Ag production in infected pretreated ME cells results from an increased synthesis of early virus **RNA**.

1981

10/3,AB/177 (Item 52 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03239299 BIOSIS NO.: 000071052410
STRINGENT-LIKE RESPONSE IN SOYBEAN GLYCINE-MAX SEEDLINGS
AUTHOR: CHEN Y-M; CHANG K T; LIN C-Y
AUTHOR ADDRESS: BOT. DEP., NATL. TAIWAN UNIV., ROC.
JOURNAL: TAIWANIA 25 (0). 1980. 18-27. **1980**
FULL JOURNAL NAME: Taiwania
CODEN: TWNAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The meristematic hook portion of soybean (Glycine max.) seedlings from 0 to 0.5 cm below cotyledones were excised and incubated in 1 mM phosphate buffer pH 6.0 or various culture media and in addition of yeast extract, coconut milk or casein hydrolysate for 12 h at 28.degree. C. Polyribosomal level (protein synthetic activity) in the tissues and the **RNA polymerase** activity in the isolated nuclei were examined. Comparison was made on the efficiency of various mediums to maintain the polyribosomal level and the **RNA polymerase** I activity in the excised hook tissues. B5 medium plus yeast extract was most effective for the maintenance of both polyribosomal level and **RNA polymerase** I activity. At the end of 12 h incubation period, **RNA polymerase** I activity was increased 40% (51% of its original activity) and polyribosomal level was increased 50% (79% of its original level). Examination of the relationship between protein synthesis and rRNA synthesis in excised root tips, 3H-leucine or 3H-uridine was used. There was a positive relationship between the protein synthetic activity and the total **RNA** synthetic activity. Total **RNA** synthesis decreased rapidly within 4 h of incubation in phosphate buffer. Much of this decrease was due to the cessation of rRNA synthesis based on use of the base **analog**, 5-fluorouracil, for inhibition of rRNA synthesis. At the end of 6 h incubation **RNA polymerase** I activity decreased to only 16% of its original activity and protein synthesis was decreased to 10% of its original level in the excised root tips. A stringent-like response may be operative in the meristematic regions of soybean seedlings.

1980

10/3,AB/178 (Item 53 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03233671 BIOSIS NO.: 000071046782
STRUCTURE ACTIVITY RELATIONSHIP SELECTIVITY AND MODE OF INHIBITION OF TERMINAL DEOXY RIBO NUCLEOTIDYL TRANSFERASE BY STREPTOLYDIGIN **ANALOGS**
AUTHOR: DICIOCCIO R A; SRIVASTAVA B I S; RINEHART K L JR; LEE V J; BRANFMAN A R; LI L-H
AUTHOR ADDRESS: DEP. EXP. THER., N.Y. STATE DEP. HEALTH, ROSWELL PARK MEML. INST., BUFFALO, N.Y. 14263, USA.
JOURNAL: BIOCHEM PHARMACOL 29 (14). 1980. 2001-2008. **1980**
FULL JOURNAL NAME: Biochemical Pharmacology
CODEN: BCPCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Three of 31 streptolydigin **analogs** resembled the parent compound in selectively inhibiting terminal deoxyribonucleotidyltransferase (terminal transferase) [a blood marker enzyme in some types of leukemia] when compared with cellular DNA **polymerases** .alpha., .beta. and .gamma., simian sarcoma virus DNA **polymerase**, herpes simplex virus-induced DNA **polymerase** and human lymphocyte **RNA polymerase** II. The other 28 compounds either did not inhibit any of these enzymes or inhibited all of these enzymes without selectivity for terminal transferase. Two **analogs** that selectively inhibited terminal transferase (Ki = 0.12 mM) were 2- to 3-fold more potent than streptolydigin (Ki = 0.32 mM). All the selective inhibitors of termininal transferase are 3-acyltetramic acids with various substitutent groups at the 1-, 3- and 5-positions. One of these, a less potent inhibitor of terminal transferase than streptolydigin, lacks the 3- and 5-substituents of streptolydigin, but has virtually the same 1-substituent. The substituent groups of the other 2 selective inhibitors are structurally different from those of streptolydigin but essentially identical to each other. The mode of inhibition of terminal transferase by selective inhibitors was the same as for streptolydigin, but different from an **analog** which non-selectively inhibited terminal transferase. Evidence suggested that the selective inhibitors specifically interacted with terminal transferase and not with initiator (oligo- or polydeoxyribonucleotide), substrate (deoxyribonucleoside 5'-triphosphates), or the divalent cation (Mn2+) required for enzyme activity. Apparently, compounds bind to the enzyme at a site(s) other than the initiator or substrate binding sites. In contrast, an **analog** which non-selectively inhibited terminal transferase apparently interacted with many proteins and polydeoxyribonucleotides non-specifically. Such inhibitors may be of value for the treatment of leukemia exhibiting abnormal terminal transferase activity.

1980

10/3,AB/179 (Item 54 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03045457 BIOSIS NO.: 000070071075
A MODEL FOR TRANSCRIPTION TERMINATION SUGGESTED BY STUDIES ON THE TRP ATTENUATOR IN-VITRO USING BASE **ANALOGS**
AUTHOR: FARNHAM P J; PLATT T
AUTHOR ADDRESS: DEP. MOL. BIOPHYS. BIOCHEM., YALE UNIV., NEW HAVEN, CONN. 06510, USA.
JOURNAL: CELL 20 (3). 1980. 739-748. **1980**
FULL JOURNAL NAME: Cell
CODEN: CELLB
RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: In vitro, termination of transcription at the attenuator site of the Escherichia coli tryptophan (trp) operon occurs efficiently in the absence of additional factors. In contrast, an altered attenuator site created by the deletion trp.DELTA.LC1419 (which removes 4 of the 8 consecutive TA base pairs at the termination site, but still functions partially in vivo) does not cause termination in vitro under standard conditions, even with the addition of rho factor. By varying components and conditions of the transcription reactions, conditions were found under which termination does occur at the altered site (trp a1419), and conditions affecting termination on the wild-type template. **RNA polymerase** can terminate at trp a1419 when the **analog** iodo-CTP (which forms stronger base pairs with G) replaces CTP. A mutant **polymerase** (rpo203) that restores termination in strains carrying rho mutations can also terminate at trp a1419, at a position just past the deletion junction; this suggests that the point of termination may be specified by the remaining upstream leader sequence. **Analogs** such as Br-UTP and allylamine-UTP, which form stronger base pairs with A, elevate readthrough levels at the wild-type attenuator site. At low temperatures, readthrough on the wild-type template by wild-type **RNA polymerase** is enhanced; whereas the rpo203 enzyme still terminates efficiently. The results of these experiments suggest a model for termination of transcription in the absence of rho factor involving both **RNA**-**RNA** and **RNA**-DNA interaction. The response of **RNA polymerase** at a terminator site is governed by a balance between the formation or stability of a hairpin structure in the transcript, and by the strength of **polymerase**-stabilized base pairing between the distal nucleotides of the transcript and the DNA template. In more complex cases in vitro, or within the cell, formation or stabilization of these structures may also involve other regions of **RNA** and additional factors.
1980

10/3,AB/180 (Item 55 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03038727 BIOSIS NO.: 000070064345
5 6 DI CHLORO-1-BETA-D RIBOFURANOSYL BENZIMIDAZOLE RESISTANCE IN CHINESE HAMSTER AND HUMAN CELLS GENETIC AND BIOCHEMICAL CHARACTERISTICS OF THE SELECTION SYSTEM
AUTHOR: GUPTA R S; SIMINOVITCH L
AUTHOR ADDRESS: DEP. MED., MCMASTER UNIV., HAMILTON, ONT. L8N 3Z5, CAN.
JOURNAL: SOMATIC CELL GENET 6 (2). 1980. 151-170. **1980**
FULL JOURNAL NAME: Somatic Cell Genetics
CODEN: SCGTD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Stable mutants resistant to the nucleoside **analog** 5,6-dichloro-1-.beta.-D-ribofuranosyl benzimidazole (DRB), which interferes with **RNA** synthesis, were selected in Chinese hamster ovary (CHO) and human diploid fibroblasts. The number of mutations induced in CHO cells treated with the mutagen ethyl methanesulfonate (EMS; 20-300 .mu.g/ml) was linearly related to the mutagen dose. The selection system did not show cell density or cross-feeding effects, and the optimal expression time following mutagenesis was 2-3 days for CHO cells and 5-6 days for human fibroblasts. The DrbR mutation behaved codominantly in DrbR .times. DrbS hybrids. Addition of DRB affected nucleoside uptake to a similar extent in both wild-type and mutant cells, indicating that the drug was able to enter the mutant cells. The failure of DrbR mutants to show any cross-resistance to other toxic nucleoside

analogs examined suggests that the action of DRB does not involve the initial phosphorylation step. DRB addition did not cause any marked inhibition of either **RNA polymerase** I or **RNA polymerase** II activity from both wild-type and mutant cells in vitro, indicating that its effect on **RNA** synthesis may be indirect.

1980

10/3,AB/181 (Item 56 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03025043 BIOSIS NO.: 000070050661
TRANSCRIPTION OF CLONED DNA FROM BACILLUS-SUBTILIS PHAGE SPO-1 REQUIREMENT FOR HYDROXYMETHYL URACIL CONTAINING DNA BY PHAGE MODIFIED **RNA POLYMERASE**
AUTHOR: LEE G; HANNETT N M; KORMAN A; PERO J
AUTHOR ADDRESS: BIOL. LAB., HARV. UNIV., CAMBRIDGE, MASS. 02138, USA.
JOURNAL: J MOL BIOL 139 (3). 1980. 407-422. **1980**
FULL JOURNAL NAME: Journal of Molecular Biology
CODEN: JMOBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Endonuclease restriction fragments of B. subtilis phage SPO1 DNA were cloned in a phage .lambda. vector, thereby replacing 5-hydroxymethyluracil (the thymine **analog** in SPO1 DNA) with thymine. Two cloned fragments contained phage SPO1 early genes. These cloned DNA, and the 5-hydroxymethyluracil-containing fragments from which they were derived, supported specific **RNA** synthesis by B. subtilis **RNA polymerase**. Two other cloned DNA contained phage middle genes, sequences that are transcribed by a modified form of B. subtilis **RNA polymerase** containing a phage-coded regulatory protein (gp28) in place of the host sigma factor. The cloned middle genes failed to support specific **RNA** synthesis by phage-modified **polymerase** although the corresponding 5-hydroxymethyluracil-containing fragments were effective templates for in vitro trsnscription. This difference in the template activity of cloned and native SPO1 fragments could not be attributed to promoter mutations introduced during replication in Escherichia coli as the nucleotide sequence of a middle gene promoter was identical for both thymine and 5-hydroxymethyluracil-containing DNA. At least under certain conditions of in vitro **RNA** synthesis, 5-hydroxymethyluracil is required for specific transcription by gp28-containing **RNA polymerase**.

1980

10/3,AB/182 (Item 57 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03025027 BIOSIS NO.: 000070050645
ROLE OF ATP IN IN-VITRO VACCINIA VIRUS **RNA** SYNTHESIS EFFECTS OF ADENOSINE 5'-BETA-GAMMA IMIDO TRI PHOSPHATE AND ADENOSINE 5'-O-3 THIO TRI PHOSPHATE
AUTHOR: SHUMAN S; SPENCER E; FURNEAUX H; HURWITZ J
AUTHOR ADDRESS: CANCER DIV. BIOL., DEP. DEV. BIOL., ALBERT EINSTEIN COLL. MED., NEW YORK, N.Y. 10461, USA.
JOURNAL: J BIOL CHEM 255 (11). 1980. 5396-5403. **1980**
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effects of the ATP **analogs**, .beta.-.gamma.-imido ATP (AMP-PNP) and .gamma.-thiophosphate ATP (ATP.gamma.S), on vaccinia transcription were examined. In vitro synthesis of **RNA** by permeabilized vaccinia virions was completely inhibited by replacement of ATP with the nonhydrolyzable **analog** AMP-PNP. The initiation of **RNA** chains, as measured by virion-catalyzed ribonucleoside triphosphate-pyrophosphate exchange, was unaffected by .beta.-.gamma.-imido ATP, but the elongation of initiated chains was prevented by substitution of the imido **analog** for ATP. ATP.gamma.S contains a S atom in place of an O2 of the .gamma.-phosphate group. Unlike AMP-PNP, the thiophosphate compound is not inherently resistant to hydrolysis. Substitution of ATP.gamma.-S for ATP completely prevented vaccinia transcription, yet substitution of GTP.gamma.S for GTP was without effect. ATP.gamma.S was readily incorporated into **RNA** by the viral transcription system in the presence of ATP or dATP, but not in the presence of AMP-PNP, suggesting that ATP.gamma.S is an effective substrate for the polymerization reaction but is not able to participate in the hypothetical mechanism that couples transcription to ATP hydrolysis. Studies on purified vaccinia enzymes revealed that the viral DNA-dependent **RNA polymerase** was fully capable of utilizing ATP.gamma.S in place of ATP. The nucleic acid-dependent phosphohydrolase II was capable of hydrolyzing ATP.gamma.S to ADP, although at a reduced rate relative to ATP hydrolysis. In contrast, nucleic acid-dependent phosphohydrolase I was incapable of cleaving ATP.gamma.S. These data provide further evidence that the requirement for a hydrolyzable .gamma.-phosphate in ATP is not a property of the vaccinia **RNA polymerase**. An essential role for phosphohydrolase I in vaccinia transcription is suggested.

1980

1980

10/3,AB/183 (Item 58 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03018141 BIOSIS NO.: 000070043759
A NEW METHOD FOR DETERMINING THE NUMBER OF **RNA POLYMERASES** ACTIVE IN CHROMATIN TRANSCRIPTION
AUTHOR: OLSZEWSKI N; GUILFOYLE T J
AUTHOR ADDRESS: DEP. BOT., UNIV. MINN., ST. PAUL, MINN. 55108, USA.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 94 (2). 1980. 553-559. **1980**
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A new method is described for determining the number of **RNA** chains which are being actively propagated in an in vitro transcription system. This method employs [32P]-.alpha.-cordycepin triphosphate which terminates **RNA** chain propagation on incorporation of the nucleotide **analog** into an **RNA** transcript. This method is quicker and subject to fewer problems than end group analysis using [3H]nucleoside triphosphates. The auxin-induced increase in soybean **RNA polymerase** I activity was examined using this method. At 12, 24 and 48 h after auxin treatment, the increase in chromatin-bound **RNA polymerase** I activity is predominantly due to a greater rate of **RNA** chain elongation rather than to an increase in the number of elongating **RNA** chains.

1980

10/3,AB/184 (Item 59 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02986463 BIOSIS NO.: 000070012081
AFFINITY LABELING OF A CYSTEINE AT OR NEAR THE CATALYTIC CENTER OF ESCHERICHIA-COLI B DNA DEPENDENT **RNA POLYMERASE**
AUTHOR: MILLER J A; SERIO G F; BEAR J L; HOWARD R A; KIMBALL A P
AUTHOR ADDRESS: DEP. CHEM., UNIV. ROCHESTER, ROCHESTER, N.Y. 14627, US.A
JOURNAL: BIOCHIM BIOPHYS ACTA 612 (1). 1980. 286-294. **1980**
FULL JOURNAL NAME: Biochimica et Biophysica Acta
CODEN: BBACA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: 9-.beta.-D-Arabinofuranosyl-6-thiopurine was used to affinity label DNA-dependent **RNA polymerase** isolated from E. coli B. This substrate **analog** displayed competitive type inhibition which could be reversed by addition of a thiol reagent, such as dithiothreitol, while exposure to H2O2, a mild oxidizing agent, caused an increase in both the inhibitory and enzyme binding capability of arabinofuranosyl thiopurine. Chromatographic analysis of the products obtained by Pronase digestion of the 9-.beta.-D-arabinofuranosyl-6-[35S]thiopurine-enzyme complex suggests that disulfide bond formation occurs between the inhibitor and a cysteine residue located in or near the active center of the enzyme. In addition, polyacrylamide gel electrophoresis indicated that the arabinofuranosyl thiopurine moiety was bound to the .beta.' subunit of the enzyme.

1980

10/3,AB/185 (Item 60 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02956263 BIOSIS NO.: 000069064381
IN-VITRO SYNTHESIS OF THE FULL LENGTH COMPLEMENT OF THE NEGATIVE STRAND GENOME **RNA** OF VESICULAR STOMATITIS VIRUS
AUTHOR: TESTA D; CHANDA P K; BANERJEE A K
AUTHOR ADDRESS: DEP. CELL BIOL., ROCHE INST. MOL. BIOL., NUTLEY, N.J. 07100, USA.
JOURNAL: PROC NATL ACAD SCI U S A 77 (1). 1980. 294-298. **1980**
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Under the normal conditions of in vitro **RNA** synthesis, the virion-associated **RNA polymerase** of vesicular stomatitis virus synthesizes 5 monocistronic mRNA and a 48-nucleotide-long leader **RNA** that represents the exact 3'-terminal region of the genome **RNA**. When the transcribing core was preincubated with ATP and CTP, reisolated, and then incubated in the presence of the .beta.,.gamma. imido **analog** of ATP (AdoPP[NH]P) and the 3 normal ribonucleoside triphosphates, the full-length complementary strand of the genome **RNA** was synthesized in vitro. Specific phosphorylated states of regulatory proteins may control transcription in vitro to generate the full-length plus strands.

1980

10/3,AB/186 (Item 61 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02921670 BIOSIS NO.: 000069029788
AFFINITY LABELING OF THE 3' HYDROXYL TERMINAL BINDING SITE OF THE **RNA** CHAIN ON DNA DEPENDENT **RNA POLYMERASE** FROM ESCHERICHIA-COLI
AUTHOR: ARMSTRONG V W; ECKSTEIN F
AUTHOR ADDRESS: ABT. CHEM., MAX-PLANCK-INST. EXP. MED., D-3400 GUETTINGEN, W. GER.
JOURNAL: BIOCHEMISTRY 18 (23). 1979. 5117-5122. **1979**
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Nucleoside triphosphates modified at the 3'-OH are chain terminators for **RNA polymerase**. They form inactive ternary complexes with the enzyme, poly(dT), and oligoadenylate, the stabilities of which depend upon the length of the oligonucleotide. Employing [5'-32P]p(Ap)10A, together with the reactive **analog** 3'-(bromoacetamido)-3'-deoxyadenosine triphosphate or 3'-(isothiocyanato)-2',3'-dideoxyadenosine triphosphate, and 3'-amino-3'-deoxyadenosine triphosphate, followed by cross-linking with glyoxal, **RNA polymerase** was labeled primarily at the .beta.' subunit. The latter therefore appears to contain at least in part the 3'-OH terminus of the nascent **RNA** chain when the enzyme is in the form of the ternary complex.

1979

10/3,AB/187 (Item 62 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02892877 BIOSIS NO.: 000069000993
DIFFERENTIAL EFFECTS OF CORDYCEPIN TRI PHOSPHATE AND 9-BETA-D ARABINOFURANOSYL ATP ON TRANSFER **RNA** AND 5S **RNA** SYNTHESIS IN ISOLATED NUCLEI
AUTHOR: LEONARD T B; JACOB S T
AUTHOR ADDRESS: DEP. PHARMACOL., MILTON S. HERSHEY MED. CENT., HERSHEY, PA. 17033, USA.
JOURNAL: BIOCHIM BIOPHYS ACTA 563 (1). 1979. 150-154. **1979**
FULL JOURNAL NAME: Biochimica et Biophysica Acta
CODEN: BBACA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Although cordycepin 5'-triphosphate (3'-dATP), at low concentrations, preferentially inhibits chromatin-associated poly(A) synthesis in isolated [rat liver] nuclei, higher levels of the inhibitor prevent rRNA (**RNA polymerase** I activity) and hnRNA (**RNA polymerase** II activity) synthesis in vitro. This nucleotide can also inhibit tRNA and 5 S **RNA** synthesis (**RNA polymerase** III activity). At 50-200 .mu.g/ml, 3'-dATP inhibits incorporation of [3H]UTP into tRNA and 5 S **RNA** by approximately 65%, whereas the syntheses of these **RNA** were completely blocked when [3H]GTP was used as the substrate. These data suggest the formation of poly(U) in the tRNA and 5 S **RNA** regions, which is resistant to 3'-dATP. Another ATP **analog**, Ara-ATP, which selectively inhibits poly(A) synthesis, does not block tRNA and 5 S **RNA** synthesis in isolated nuclei. The

production of these **RNA** species in isolated nuclei is also insensitive to Ara-CTP and 2'dATP. 3'-dATP apparently exerts general inhibitory effects on **RNA** synthesis; and further substantiate the conclusion that Ara-ATP is a selective inhibitor of the polyadenylation reaction in vitro.

1979

10/3,AB/188 (Item 63 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02778700 BIOSIS NO.: 000018011817
THE EFFECT OF PYRO PHOSPHATE **ANALOG** ON INFLUENZA VIRUS **RNA** **POLYMERASE** AND INFLUENZA VIRUS MULTIPLICATION
AUTHOR: STRIDH S; HELGSTRAND E; LANNERO B; MISIORNY A; STENING G; OBERG B
AUTHOR ADDRESS: RES. DEV. LAB., ASTRA LAKEMEDEL AB, S-151 85 SODERTAELJE, SWED.
JOURNAL: ARCH VIROL 61 (3). 1979. 245-250. **1979**
FULL JOURNAL NAME: Archives of Virology
CODEN: ARVID
RECORD TYPE: Citation
LANGUAGE: ENGLISH
1979

10/3,AB/189 (Item 64 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02717711 BIOSIS NO.: 000068028304
INITIATION OF **RNA** SYNTHESIS IN-VITRO BY VESICULAR STOMATITIS VIRUS ROLE OF ATP
AUTHOR: TESTA D; BANERJEE A K
AUTHOR ADDRESS: DEP. CELL BIOL., ROCHE INST. MOL. BIOL., NUTLEY, N.J. 07110, USA.
JOURNAL: J BIOL CHEM 254 (6). 1979. 2053-2058. **1979**
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The ATP requirement during **RNA** transcription by the **RNA**-dependent **RNA polymerase** associated with purified vesicular stomatitis virus was studied during chain initiation and chain elongation steps. Initiation of transcription in vitro has an apparent Km for ATP of approximately 500 .mu.M; the apparent Km for ATP during chain elongation is almost identical with those for the other 3 ribonucleoside triphosphates, i.e., 20-30 .mu.M. Further analysis of the transcription process demonstrated that the .beta.-.gamma. imido **analog** of ATP cannot be used for the initiation step. It can be incorporated into **RNA** during chain elongation. A hydrolyzable form of the .beta.-.gamma. phosphodiester bond in ATP is required for the initiation process. The hypothesis for a single promoter site for the initiation of transcription on the genome of vesicular stomatitis virus was supported.

1979

10/3,AB/190 (Item 65 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02592679 BIOSIS NO.: 000017040737
QUATERNARY STRUCTURE OF ESCHERICHIA-COLI **RNA POLYMERASE**
EC-2.7.7.6 PART 1 MEASUREMENT OF DISTANCES BY FLUORESCENCE ENERGY TRANSFER
AUTHOR: STENDER W
JOURNAL: HOPPE-SEYLER'S Z PHYSIOL CHEM 359 (3). 1978 327 **1978**
FULL JOURNAL NAME: Hoppe-Seyler'S Zeitschrift fuer Physiologische Chemie
CODEN: HSZPA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
1978

10/3,AB/191 (Item 66 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02487961 BIOSIS NO.: 000066070518
TRANSCRIPTION OF PHAGE T-7 DNA CONTAINING MODIFIED NUCLEOTIDES BY BACTERIO PHAGE PHAGE T-7 SPECIFIC **RNA POLYMERASE**
AUTHOR: STAHL S J; CHAMBERLIN M J
AUTHOR ADDRESS: DEP. BIOCHEM., UNIV. CALIF., BERKELEY, CALIF. 94720, USA.
JOURNAL: J BIOL CHEM 253 (14). 1978 4951-4959. **1978**
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The interaction of bacteriophage T7 specific **RNA polymerase** with its cognate promoter sites was probed by selectively replacing bases in one T7 promoter site with base **analogs**. Base **analogs** such as 2,6-diaminopurine or hypoxanthine, which alter residues appearing in the minor groove of the DNA helix, prevent utilization of the promoter by T7 **RNA polymerase**. These **analogs** do not affect transcription which starts outside of the modified region. Base **analogs** that have alterations that appear in the major groove of the DNA helix, such as uracil, 5-bromouracil, 5-methylcytosine, 5-hydroxymethylcytosine and [5-HgSR]pyrimidines, do not prevent utilization of the promoter. The deoxyribonucleoside **analog** 5'-imino-5'-deoxythymidine, an alteration appearing in the deoxyribosephosphodiester backbone of the DNA helix, does not prevent promoter recognition. Haemophilus aegyptius restriction endonuclease [Hae-] III, which cleaves DNA at the sequence 5'GGCC3', does not act at sites in which the guanine residues in 1 of the 2 DNA strands were substituted with hypoxanthine. This implicates the guanine amino group in the minor groove of the DNA helix as a possible recognition point for this restriction endonuclease.

1978

10/3,AB/192 (Item 67 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02473604 BIOSIS NO.: 000066056150
SYNTHESIS AND PROPERTIES OF A NEW FLUORESCENT **ANALOG** OF ATP ADENOSINE 5 TRI PHOSPHORO-GAMMA-1-5-SULFONIC-ACID NAPHTHYLAMIDATE
AUTHOR: YARBROUGH L R
AUTHOR ADDRESS: DEP. BIOCHEM., KANS. UNIV. MED. CENT., KANSAS CITY, KANS. 66103, USA.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 81 (1). 1978 35-41. **1978**
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: An **analog** of ATP was synthesized which contains the fluorophore, 1-aminonaphthalene-5-sulfonate attached via a .gamma.-phosphoamidate bond. This **analog** is strongly fluorescent (quantum yield = 0.63) with an emission maximum at 460 nm; the excited state lifetime is 20 ns. It is a substrate for DNA-dependent **RNA polymerase** of Escherichia coli and wheat germ **RNA polymerase** II. It is also a substrate for E. coli valyl tRNA synthetase, venom phosphodiesterase and potato apyrase. Cleavage of the .alpha.-.beta. phosphoryl bond as a result of **RNA** synthesis or by venom phosphodiesterase produces a 15 nm red shift in the fluorescence emission spectrum. This property should make this nucleotide useful for studies of the mechanisms of enzymatic reactions involving cleavage of the .alpha.-.beta. phosphoryl bond.

1978

10/3,AB/193 (Item 68 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02438574 BIOSIS NO.: 000066021117
TERMINATION OF TRANSCRIPTION BY ESCHERICHIA-COLI **RNA POLYMERASE** IN-VITRO IS AFFECTED BY RIBO NUCLEOSIDE TRI PHOSPHATE BASE **ANALOGS**
AUTHOR: NEFF N F; CHAMBERLIN M J
AUTHOR ADDRESS: DEP. BIOCHEM., UNIV. CALIF., BERKELEY, CALIF. 94720, USA.
JOURNAL: J BIOL CHEM 253 (7). 1978 2444-2460. **1978**
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: E. coli **RNA polymerase** holoenzyme transcribes bacteriophage T7 DNA selectively in vitro. Under normal conditions transcription is initiated predominantly at the 3 A promoter sites (near 1% on the standard genetic map) and is terminated at a site located at 20%. Transcription of DNA from the homologous bacteriophage T3 is also initiated predominantly at the left end of the genetic map, but where transcription is terminated near 20% in vivo, there is little or no termination in vitro. Ribonucleoside triphosphate base **analogs** can be incorporated into the **RNA** chain which alter the stability of the **RNA**-DNA hybrid made during transcription and substantially affect termination at the 2 termination sites in vitro. Substitution of a ribonucleoside triphosphate base **analog** (5-bromocytidine-5'-triphosphate) which stabilizes the **RNA**-DNA hybrid stimulates termination with T3 DNA. Substitution of a base **analog** (ITP) that destabilizes the **RNA**-DNA hybrid supresses termination with T7 DNA. These 2 observations suggest that the critical step in the termination of transcription is the formation of a G-C containing **RNA**-DNA hybrid at the termination site. This model is supported by transcription studies on synthetic homopolymers (dGn) .cntdot. (dCn) and d(A-T)n. **RNA polymerase** appears to terminate and reinitiate frequently when (dG) .cntdot. (dCn) is transcribed with GTP and a stable **RNA**-DNA hybrid (rG) .cntdot. (dCn) is found. Termination occurs rarely, however, when d(A-t)n is the template or when ITP is the substrate for (dGn) .cntdot. (dCn) transcription and a free **RNA** chain is formed. It appears that the termination of transcription is stimulated when the formation of a stable **RNA**-DNA hybrid is favored over the reformation of the DNA duplex.

1978

10/3,AB/194 (Item 69 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02415029 BIOSIS NO.: 000065072072
SYNTHESIS OF PHENAZINE AND PHENOXAZINONE DERIVATIVES OF GELDANAMYCIN AS POTENTIAL **POLYMERASE** INHIBITORS
AUTHOR: RINEHART K L JR; MCMILLAN M W; WITTY T R; TIPTON C D; SHIELD L S; LI L H; REUSSER F
AUTHOR ADDRESS: ROGER ADAMS LAB., UNIV. ILL., URBANA, ILL. 61801, USA.
JOURNAL: BIOORG CHEM 6 (3). 1977 353-370. **1977**
FULL JOURNAL NAME: Bioorganic Chemistry
CODEN: BOCMB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Derivatives of geldanamycin, phenazines and phenoxazinones, some of them **analogous** to rifazine in the rifamycin series, were synthesized. Most of the geldanamycin derivatives were effective inhibitors of **RNA**-dependent DNA **polymerase** from Rauscher leukemia virus. A simple **analog** containing the aromatic chromophore of the derivatives but without the ansa ring also showed viral inhibition.

1977

10/3,AB/195 (Item 70 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02410235 BIOSIS NO.: 000065067278
SACCHAROMYCES-CEREVISIAE DNA DEPENDENT **RNA POLYMERASE** III A ZINC METALLO ENZYME
AUTHOR: WANDZILAK T M; BENSON R W
AUTHOR ADDRESS: DEP. BIOCHEM., SCH. DENT., UNIV. LOUISVILLE, LOUISVILLE, KY. 40232, USA.
JOURNAL: BIOCHEMISTRY 17 (3). 1978 426-431. **1978**
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Yeast nuclear **RNA polymerase** III was purified by batch adsorption to phosphocellulose, followed by ion-exchange chromatography on DEAE-Sephadex and affinity chromatography on DNA-Sepharose. Polyacrylamide gel electrophoresis of the purified enzyme showed a single protein band which contained **polymerase** activity. The MW estimated by sedimentation velocity centrifugation in a glycerol gradient was 380,000. Enzyme activity was inhibited 50% at 0.1 mM 1,10-phenanthroline and 100% at 1.0 mM, but was restored when 1,10-phenanthroline was removed by dialysis. Enzyme activity was not inhibited by 7,8-benzoquinoline, a nonchelating structural **analog** of 1,10-phenanthroline. These results strongly suggest that inhibition of enzyme activity occurs by the formation of a reversible enzyme-zinc-phenanthroline ternary complex. The zinc content, measured by atomic absorption spectroscopy, was 2 g-atoms per mol of enzyme. Zn was not removed from the enzyme by gel filtration on Sephadex G-25, by passage through Chelex-100 resin, or by dialysis against buffer containing 1,10-phenanthroline. Enzyme-bound Zn was removed by dialysis after denaturation of the enzyme with heat and sodium dodecyl sulfate. Enzyme-bound Zn did not exchange with free Zn. These results establish

yeast nuclear **RNA polymerase** III as a Zn metalloenzyme.

1978

10/3,AB/196 (Item 71 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02376299 BIOSIS NO.: 000065033330
ROLE OF THE INTRINSIC METAL IN **RNA POLYMERASE** EC-2.7.7.6 FROM ESCHERICHIA-COLI IN-VIVO SUBSTITUTION OF TIGHTLY BOUND ZINC WITH COBALT
AUTHOR: SPECKHARD D C; WU F Y-H; WU C-W
AUTHOR ADDRESS: DIV. BIOL. SCI., DEP. BIOPHYS., ALBERT EINSTEIN COLL. MED., NEW YORK, N.Y. 10461, USA.
JOURNAL: BIOCHEMISTRY 16 (24). 1977 5228-5233. **1977**
FULL JOURNAL NAME: Biochemistry
CODEN: BICHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: E. coli **RNA polymerase** [EC 2.7.7.6] is a metalloenzyme containing 2 g-atoms of tightly bound Zn/mol of enzyme. **RNA polymerase** from E. coli cells grown in a Zn-depleted medium supplemented with CoCl2 was prepared. The purified enzyme contains 1.8 .apprx. 2.2 g-atoms of Co/mol of enzyme with concomitant reduction in the Zn content. The Co-substituted enzyme is enzymatically as active as Zn-**RNA polymerase** on a variety of templates under standard assay conditions. These 2 enzymes are almost identical by such physical criteria as subunit composition, monomer-dimer equilibrium and pH and temperature stabilities. They differ in that Co-**RNA polymerase** exhibits a visible absorption spectrum with 2 major peaks at 584 and 703 nm. Addition of nucleoside triphosphates selectively perturbs the 584 nm peak, but the addition of a template **analog**, d(pT)10, affects both peaks. These spectral changes suggest that the tightly bound metal ions may directly or indirectly participate in binding of substrate or template to the enzyme. Biochemically, both enzymes are also very similar with respect to pH-activity profile, extrinsic metal requirements, 1,10-phenanthroline inhibition and fidelity of transcription of synthetic templates. Detailed kinetic and biochemical analyses revealed that the Co enzyme has a lower value (.apprx. 2-fold) of apparent Km for [phage] T7 DNA under certain experimental conditions and that it is less efficient in initiating **RNA** chains at the A2 than at the A1 + A3 promoters on T7 DNA template as compared to the Zn enzyme. This was demonstrated by studying the ratio of GTP/ATP incorporations into the 5' terminal of **RNA** products and by measuring the formation of (rI)n-resistant initiation complexes at specific promoter sites using various combinations of dinucleotides and nucleoside triphosphates. The in vitro transcription of a lac operon system by Co-**RNA polymerase** is less sensitive to c[cyclic]AMP and cAMP receptor protein than is the transcription by Zn-**RNA polymerase**. The results of comparative studies using the Co and Zn enzymes showed that the intrinsic metal of **RNA polymerase** is apparently involved in promoter recognition and specific initiation in **RNA** synthesis.

1977

10/3,AB/197 (Item 72 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02353356 BIOSIS NO.: 000065010373

EFFECT OF CORDYCEPIN ON NUCLEIC-ACID METABOLISM IN L-5178Y CELLS AND ON NUCLEIC-ACID SYNTHESIZING ENZYME SYSTEMS
AUTHOR: MUELLER W E G; SEIBERT G; BEYER R; BRETER H J; MAIDHOF A; ZAHN R K
AUTHOR ADDRESS: INST. PHYSIOL. CHEM., JOHANN JOACHIM BECHER WEG 13, 65 MAINZ, W. GER.
JOURNAL: CANCER RES 37 (10). 1977 3824-3833. **1977**
FULL JOURNAL NAME: Cancer Research
CODEN: CNREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Cordycepin [3'-deoxyadenosine (3'-dAdo)] is an adenosine **analog** that interferes with nucleic acid synthesis in vivo and in vitro. In vivo studies were performed with L5178Y [mouse leukemia] cells. 3'-dAdo inhibited cell proliferation (concentration that induces 50% inhibition of cell proliferation, 0.27 .mu.M); 3'-dAdo-treated cells did not show unbalanced growth. The inhibitory potency of 3'-dAdo could be abolished to some extent by coincubation with adenosine, but not with 2'-deoxyadenosine. In precursor studies, 3'-dAdo reduced protein synthesis and to a lesser extent, total **RNA** synthesis. The reduction of protein synthesis was probably the result of inhibition of mRNA synthesis, since in the presence of 3'-dAdo the number of polysomes decreased. In an intact cell system, [3H]-3'-dAdo was incorporated into **RNA** but not into DNA. Incorporated [3H]-3'-dAdo was found in the polyadenylate [poly(A)] stretch of poly(A)-containing **RNA** and in the 10 S and 55 S species of poly(A)-free **RNA**. Cordycepin triphosphate (3'dATP) had no influence on the activity of DNA dependent DNA **polymerase** .alpha. and .beta. from L5178y cells. The incorporation rate of ATP into **RNA** by DNA dependent **RNA** **polymerases** I, II and III from mouse liver was moderately inhibited by 3'-dATP. The strongest inhibitory effect of 3'-dATP was observed in the enzyme systems containing nuclear poly(A) **polymerase** (from oviduct) or cytoplasmic terminal riboadenylate transferase (from calf thymus). The inhibition type was competitive with respect to ATP. In the case of poly(A) **polymerase** and terminal riboadenylate transferase, enzyme activity was also inhibited competitively with respect to the oligo(pA)10 initiator. 3'-dATP was used as substrate by poly(A) **polymerase**. Incorporated cyclic dAMP acted as chain terminator.

1977

10/3,AB/198 (Item 73 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02255853 BIOSIS NO.: 000014025868
EFFECT OF L AMINOETHYL CYSTEINE A SULFUR **ANALOG** OF L LYSINE ON VIRUS MULTIPLICATION IN MAMMALIAN CELL CULTURES
AUTHOR: SCIOSCIA-SANTORO A; CAVALLINI D; DEGENER A M; PEREZ-BERCOFF R; RITA G
JOURNAL: EXPERIENTIA (BASEL) 33 (4). 1977 451-453 **1977**
FULL JOURNAL NAME: EXPERIENTIA (Basel)
CODEN: EXPEA
RECORD TYPE: Citation
1977

10/3,AB/199 (Item 74 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02183979 BIOSIS NO.: 000064026493
5-PRIME TERMINI OF REOVIRUS MESSENGER **RNA** ABILITY OF VIRAL CORES TO

FORM CAPS POST TRANSCRIPTIONALLY
AUTHOR: FURUICHI Y; SHATKIN A J
JOURNAL: VIROLOGY 77 (2). 1977 566-578. **1977**
FULL JOURNAL NAME: Virology
CODEN: VIRLA
RECORD TYPE: Abstract

ABSTRACT: The 5'-terminal cap structure of reovirus mRNA, m7GpppGm-C, is synthesized by 5 coordinate reactions that involve the sequential action of the virion-associated **RNA polymerase**, nucleotide phosphohydrolase, guanylyltransferase and 2 distinct methyltransferases. Caps are synthesized in vitro by viral cores at an early stage of transcription. Under appropriate conditions cap formation can also occur post-transcriptionally. Preformed, nascent mRNA with 5'-terminal ppG-C was modified to m7GpppGm-C by guanylyl- and methyltransferases under conditions that prevented further **RNA** synthesis and chain completion, indicating that the transferases and **RNA polymerase** activities are not tightly coupled within cores. Similarly, the **polymerase** appears to be independent of the **RNA** 5'-modifying enzymes, since transcription occurred in the presence of the imido **analog** of GTP, GMP-PNHP [5'-guanylyl-imidodiphosphate], yielding **RNA** with a 5'-terminal triphosphate structure, p(NH)ppG-C. The imido linkage of the .beta.- and .gamma.-phosphates was not cleaved by the nucleotide phosphohydrolase, consequently preventing the formation of diphosphate-containing 5'-termini required for the synthesis of GpppG-C by guanylate transfer. Unlike its inactivity as a GMP acceptor, GMP-PNHP was utilized as a GMP donor for conversion of ppG-C termini to GpppG-C by reovirus cores, consistent with the proposed mechanism of cap synthesis.

1977

10/3,AB/200 (Item 75 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02148840 BIOSIS NO.: 000063063843
THE STEREOCHEMICAL BASIS OF TEMPLATE FUNCTION
AUTHOR: RACKWITZ H R; SCHEIT K H
JOURNAL: EUR J BIOCHEM 72 (1). 1977 191-200. **1977**
FULL JOURNAL NAME: European Journal of Biochemistry
CODEN: EJBCA
RECORD TYPE: Abstract

ABSTRACT: The behavior of nucleotides with thioketo-substituted pyrimidine bases (4-thiouracil,2-thiouracil and 2-thiocytosine) or amino-**analog** purine bases (2-aminopurine and 2,6-diaminopurine) in transcription and translation was investigated. The stereochemical basis of substrate selection in transcription is the geometry of Watson-Crick base pairs A.cntdot.U (or A.cntdot.T) and G.cntdot.C between substrate and template bases. The topology of the active site of Escherichia coli **RNA polymerase** [EC 2.7.7.6] is precisely adopted to the geometry of Watson-Crick base pairs. The enzyme active site discriminates between A.cntdot.U (A.cntdot.T) and G.cntdot.C base pairs. An essential feature in this discrimination is the 6-NH2 group of the A.cntdot.U (A.cntdot.T) base pair and the 2-keto group of cytosine in the G.cntdot.C base pair. The codon properties of a nucleic acid base in mRNA can be predicted on the basis of its specificity in polynucleotide interactions. There seems to be no evidence for the participation of protein topological sites in the control of the specificity of codon-anticodon interactions in translation.

1977

10/3,AB/201 (Item 76 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02119992 BIOSIS NO.: 000063034988
STEREOCHEMISTRY OF POLYMERIZATION BY DNA DEPENDENT **RNA** **POLYMERASE** EC-2.7.7.6 FROM ESCHERICHIA-COLI AN INVESTIGATION WITH A DIA STEREOMERIC ATP **ANALOG**
AUTHOR: ECKSTEIN F; ARMSTRONG V W; STERNBACH H
JOURNAL: PROC NATL ACAD SCI U S A 73 (9). 1976 2987-2990. **1976**
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract

ABSTRACT: The phosphodiester bond formation by DNA-dependent **RNA**-**polymerase** (**RNA** nucleotidyltransferase, nucleosidetriphosphate:**RNA** nucleotidyltransferase, EC 2.7.7.6) [of E. coli] can in principle result in retention, inversion or racemization of configuration at the .alpha.-P of the nucleoside 5'-triphosphate being polymerized. As a 1st step in elucidating the sterochemistry of this reaction, 1 diastereomer (A) of adenosine 5'-O-(1-thiotriphosphate) (ATP.alpha.S) was polymerized with UTP in the presence of poly(dA-dT.cntdot.poly(dA-dT). The resulting polymer was enzymatically cleaved to uridine 2',3'-cyclic phosphorothioate which was determined to be the endo-isomer by comparison with an authentic sample. This shows that no racemization occurred and that isomer A of ATP.alpha.S gives a phosphorothioate diester bond with the R-configuration. Whether this represents inversion or retention of configuration awaits elucidation of the absolute configuration of isomer A for ATP.alpha.S.

1976

10/3,AB/202 (Item 77 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02088292 BIOSIS NO.: 000063003276
INHIBITION OF MAMMALIAN POLY ADENYLATE **POLYMERASE** BY 2 AZA-1 N-6 ETHENO ATP
AUTHOR: KESHGEGIAN A A; TSOU K C; FURTH J J
JOURNAL: CANCER RES 36 (9). 1976 3151-3155. **1976**
FULL JOURNAL NAME: Cancer Research
CODEN: CNREA
RECORD TYPE: Abstract

ABSTRACT: 2-Aza-1,N6-etheno-ATP (aza-.epsilon.ATP), a fluorescent **analog** of ATP, significantly inhibits polyadenylate [poly(A)] **polymerase** of bovine lymphosarcoma and calf thymus, with 50% inhibition at 200 .mu.M (in the presence of an equal concentration of ATP). Calf thymus **RNA polymerase** II and III are inhibited 32 and 20%, respectively, by a 3.8 fold excess of aza-.epsilon.ATP. DNA **polymerase** .alpha. is not inhibited. The inhibition of poly(A) **polymerase** by aza-.epsilon.ATP appears to be competitive with ATP. Incorporation of aza-.epsilon.ATP is not observed. Polymers of 2-aza-1,N6-etheno-AMP are used as primers, but poorly. 1,N-Etheno-ATP and 9-.beta.-D-arabinofuranosyl-ATP are poor inhibitors of poly(A) **polymerase**. ADP is ineffective. dATP inhibits to the same extent as aza-.epsilon.ATP, while other naturally occurring nucleotides inhibit poly(A) **polymerase** to varying degrees, with deoxynucleoside triphosphates more potent than ribonucleoside triphosphates. Inhibition

of poly(A) **polymerase** by naturally occurring nucleoside triphosphates suggests that nucleotides may regulate the enzyme in vivo. Inhibition by the fluorescent **analog** aza-.epsilon.ATP suggests that this compound may be useful in elucidating poly(A) metabolism in normal and neoplastic cells.

1976

10/3,AB/203 (Item 78 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01929660 BIOSIS NO.: 000062019754
A STUDY OF POSSIBLE MECHANISMS OF THE **RNA POLYMERASE** INVOLVEMENT IN MUTAGENESIS IN PHAGE T-4
AUTHOR: PIRUZIAN E S; ALIKHANIAN S I; YAROSLAVTSEVA N G
JOURNAL: MUTAT RES 35 (1). 1976 1-6. **1976**
FULL JOURNAL NAME: Mutation Research
CODEN: MUREA
RECORD TYPE: Citation
1976

10/3,AB/204 (Item 79 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01919404 BIOSIS NO.: 000062009498
THE EFFECT OF EMBICHIN AND OF ITS MONO FUNCTIONAL **ANALOG** ON THE MATRIX OF CHROMATIN AND DNA IN THE **RNA POLYMERASE** SYSTEM IN-VITRO
AUTHOR: SOKOLOV N A; PIKER E G; MIRONOV N M; TSEITLIN P I
JOURNAL: BYULL EKSP BIOL MED 80 (8). 1975 106-109. **1975**
FULL JOURNAL NAME: Byulleten' Eksperimental'noi Biologii i Meditsiny
CODEN: BEBMA
RECORD TYPE: Abstract

ABSTRACT: The antitumor agent embichin inhibited the matrix activity of calf thymus chromatin and DNA in the **RNA polymerase** system in vitro more than its monofuctional **analog**. Chromatin possessed a greater sensitivity to the action of embichin in comparison with the deproteinized DNA. A monofuctional embichin **analog** showed a greater reduction of matrix DNA activity in comparison with chromatin. The depression mechanism of the matrix activity of chromatin with the action of embichin was apparently associated with the capacity of the latter to form DNA-protein bonds in the chromatin composition.

1975

10/3,AB/205 (Item 80 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01825028 BIOSIS NO.: 000012085088
EFFECT OF MUSTINE AND ITS MONO FUNCTIONAL **ANALOG** ON TEMPLATE ACTIVITY OF CHROMATIN AND DNA IN AN **RNA POLYMERASE** SYSTEM IN-VITRO
AUTHOR: SOKOLOV N A; PIKER E G; MIRONOV N M; TSEITLIN P I
JOURNAL: BULL EXP BIOL MED (ENGL TRANSL BYULL EKSP BIOL MED) 80 (8). 1975 (1976) 975-978 **1975 1976**
FULL JOURNAL NAME: Bulletin of Experimental Biology and Medicine (English Translation of Byulleten' Eksperimental'noi Biologii i Meditsiny)
CODEN: BEXBA

RECORD TYPE: Citation
1975 1976

10/3,AB/206 (Item 81 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

00939063 BIOSIS NO.: 000053059253
MECHANISM OF ACTION OF AMODIAQUINE SYNTHESIS OF ITS INDOLO QUINOLINE **ANALOG**
AUTHOR: MARQUEZ V E; CRANSTON J W; RUDDON R W; KIER L B; BURCKHALTER J H
JOURNAL: J MED CHEM 15 (1). 1972 36-39. **1972**
FULL JOURNAL NAME: Journal of Medicinal Chemistry
CODEN: JMCMA
RECORD TYPE: Citation
1972
?

supra). Both 2'-amino and 2'-fluoro nucleoside 5-triphosphates are substrates for T7 RNA polymerase, albeit with somewhat decreased incorporation efficiency (Aurup et al. (1992) Biochemistry 31',9636-9641). Other 2'-substituted nucleotides such as 2'-O-methyl, 2'-O-alkyl, or 2'-deoxy nucleoside 5-triphosphates are not recognized as substrates by T7 RNA polymerase.

BSPR:
The oligonucleotide ligands of the present invention may have one or more X-modified bases, or one or more Y-modified bases, or a combination of X- and Y-modified bases. The present invention encompasses derivatives of these substituted pyrimidines and purines such as 5'-triphosphates, and 5'-dimethoxytrityl, 3'-.beta.-cyanoethyl, N, N-diisopropyl phosphoramidites with isobutyrl protected bases in the case of adenosine and guanosine, or acyl protection in the case of cytosine. Further included in the present invention are oligonucleotides bearing any of the nucleotide analogs herein disclosed. The present invention encompasses specific nucleotide analogs modified at the 5 and 2' positions, including 5-(3-aminoallyl)uridine triphosphate (5-AA-UTP), 5-(3-aminoallyl) deoxyuridine triphosphate (5-AA-dUTP), 5-fluorescein-12-uridine triphosphate (5-F-12-UTP), 5-digoxygenin-11-uridine triphosphate (5-Dig-11-UTP), 5-bromouridine triphosphate (5-Br-UTP), 2'-amino-uridine triphosphate (2'-NH.sub.2 -UTP) and 2'-amino-cytidine triphosphate (2'-NH.sub.2 -CTP), 2'-fluoro-cytidine triphosphate (2'-F-CTP), and 2'-fluoro-uridine triphosphate (2'-F-UTP).

DRPR:
FIG. 2 illustrates the structures of 5-allylamino-UTP (5-AA-UTP), 5-bromo-UTP (5-Br-UTP), 5-fluorescein-12-UTP (5-F-12-UTP), 5-digoxygenin-11-UTP (5-Dig-11-UTP).

DRPR:
FIGS. 7A-7F show proposed secondary structures of RNA ligands.

DRPR:
FIG. 10 shows the synthesis of 2'-amino,2'-deoxyuridine 5'-triphosphate.

DEPR:
1) A candidate mixture of nucleic acids of differing sequence is prepared. The candidate mixture generally includes regions of fixed sequences (i.e., each of the members of the candidate mixture contains the same sequences in the same location) and regions of randomized sequences. The fixed sequence regions are selected either: a) to assist in the amplification steps described below; b) to mimic a sequence known to bind to the target; or c) to enhance the concentration of a given structural arrangement of the nucleic acids in the candidate mixture. The randomized sequences can be totally randomized (i.e., the probability of finding a base at any position being one in four) or only partially randomized (e.g., the probability of finding a base at any location can be selected at any level between 0 and 100 percent).

DEPR:
Introduction of 2'-amino,2'-deoxy pyrimidines into the SELEX candidate mixture library requires preparation of their 5'-triphosphate derivatives. This is the form that is recognized as a substrate for DNA-dependent RNA polymerases or for DNA-dependent DNA polymerases. Furthermore, analogs also have to be prepared as the phosphoramidite in order to be incorporated into the final oligonucleotide ligand by automated chemical synthesis. These derivatives have been described, along with their method of preparation (Aurup et al. (1992) Biochemistry 31:9636). The synthesis of oligonucleotides containing 2'-amino,2'-deoxy pyrimidines by T7 RNA polymerase transcription of DNA templates has also been previously reported (Aurup et al. (1992) supra; Pieken et al. (1990) supra). Homopolymers of the 2'-amino,2'-deoxy pyrimidine nucleotides have also been prepared by polymerization of their 5'-diphosphate derivatives (Hobbs et al. (1973) supra). oligoribonucleotides containing 2'-amino,2'-deoxy pyrimidines have also been prepared by automated solid phase synthesis. The trifluoroacetyl group has been used for protection of the 2'-amino group in preparation of phosphoramidite monomers (Pieken et al. (1990) supra).

DEPR:
As described above and in the SELEX patent applications, the SELEX technology identifies specific high affinity oligonucleotide ligands to a given molecular

target by iterative enrichment from a vast pool of species. In one embodiment of the present invention, the amplified oligodeoxyribonucleotide sequences are transcribed to its oligoribonucleotide homolog with T7 RNA polymerase. Thus, during each step in the enrichment process, the library is reassembled from its nucleoside triphosphate building blocks. This feature allows the introduction of chemically modified nucleoside triphosphates, and thus the enrichment of ligands bearing chemical functionalities not found in native RNA. Examples of such modifications include chemical substitutions at the ribose and/or phosphate positions of a given RNA sequence. See, e.g., Cook et al. PCT Application WO 9203568; U.S. Pat. No. 5,118,672 of Schinazi et al.; Hobbs et al. (1973) Biochem 12:5138; Guschlbauer et al.(1977) Nucleic Acids Res. 4:1933; Shibahara et al. (1987) Nucl. Acids. Res. 15:4403; Pieken et al. (1990) supra, each of which is specifically incorporated herein by reference.

DEPR:
5-iodo-2'-amino, 2'-deoxyuridine has been prepared previously (Verheyden et al. (1971) J. Org. Chem. 36:250). It has not been applied to the uses discussed herein. The 5-iodo,2'-deoxyuridine is introduced into the SELEX library of candidate oligonucleotides as the 5'-triphosphate derivative. The 5-iodo substituent is not compatible with the reaction conditions used in standard phosphorylation of 5-iodo,2' amino,2'-deoxy pyrimidines. Instead, the 5'-triphosphate derivative, which has not been previously described, is prepared from the 2'-amino,2'-deoxy pyrimidine 5'-triphosphate by mercuration of the 5-position (Dale et al. (1975) Biochemistry 14:2447) with subsequent iodination (Dale et al. (1975) Nucleic Acids Res. 2:915). These modified bases are central intermediates in the generation of base-modified nuclease resistant oligonucleotide ligands.

DEPR:
In order to be useful in the existing SELEX protocol, the modified nucleotides must meet the following criteria: 1) in their triphosphate forms they must be substrates for polymerase(s), and 2) the resulting modified oligonucleotides must be templates for amplification. Example 2 demonstrates that four prototypic 5-modified uridines meet the above requirements and can be used in SELEX. 5-AA-UTP, 5-F-12-UTP, 5-Dig-11-UTP, and 5-Br-UTP, shown in FIG. 2, are incorporated into RNA by the T7 RNA polymerase under standard transcription conditions. Modified transcripts were reversed transcribed into cDNA by AMV reverse transcriptase and amplified by PCR. These results show that modified nucleotides can be directly incorporated into the SELEX procedure.

DEPR:
As discussed above, 2'-amino modified pyrimidines and purines exhibit increased resistance to endonuclease activity. Example 3 describes SELEX selection of 2'-NH.sub.2 ligands to the human thrombin. The affinities of SELEX identified 2'-OH and 2'-NH.sub.2 ligands to thrombin are compared. While Example 3 describes SELEX identification of RNA ligands, the same procedure may be performed for the SELEX identification of DNA ligands to a specific target molecule. The only enzymatic requirement for DNA SELEX is that the modified deoxynucleoside triphosphates serve as substrates for Taq DNA polymerase or another suitable polymerase. It is known that digoxygenin-11-deoxyuridine triphosphate can be used as a replacement substrate for TPP in PCR (Lanzillo (1990) BioTechniques 8:621).

DEPR:
As has been shown, sequences that have little or no primary sequence homology may still have substantially the same ability to bind the target molecule. It is clear that binding is controlled by the secondary or tertiary structure of the nucleic acid ligand. For these reasons, the present invention includes nucleic acid ligands that have substantially the same structural form as the ligands presented herein and that have substantially the same ability to bind thrombin as the modified and unmodified nucleic acid ligands shown in FIGS. 6A and 6B. Wherein substantially the same structure includes all nucleic acid ligands having the common structural elements shown in FIGS. 7A-7F that lead to the affinity to thrombin. This invention further includes ligands containing a variety of modified nucleotides, such as 2'-fluoro modifications.

DEPR:
Example 5 describes the synthesis of 5-iodo,2'-amino,2'-deoxy pyrimidine 5'-triphosphate. 5-iodo,2'-amino,2'-deoxy pyrimidine 5'-triphosphates cannot be prepared from their 5-iodo,2'-amino,2'-deoxy pyrimidine nucleoside precursors

because the conditions employed in the phosphorylation reaction are not compatible with the 5-iodo group. However, they may be prepared from the 2'-amino,2'-deoxy pyrimidine 5'-triphosphates by mercuration and subsequent iodination of the C-5 position.

DEPR:
The method of the present invention further includes incorporation of functional groups into oligonucleotides via the modified nucleotides. One of the products of the SELEX procedure is a consensus of primary and secondary structures that enables the chemical or enzymatic synthesis of oligonucleotide ligands whose design is based on that consensus. Because the replication machinery of SELEX requires that rather limited variation at the subunit level (ribonucleotides, for example), such ligands imperfectly fill the available atomic space of a target molecule's binding surface. However, these ligands can be thought of as high-affinity scaffolds that can be derivatized to make additional contacts with the target molecule. In addition, the consensus contains atomic group descriptors that are pertinent to binding and atomic group descriptors that are coincidental to the pertinent atomic group interactions. The present invention further includes nucleic acid ligands containing additional functional groups introduced via the modified nucleotides. A strategy for introduction of functional groups is described in Example 7.

DEPR:
Essential features of the SELEX protocol have been described in detail in previous papers (Tuerk & Gold (1990) Science 249:505; Tuerk et al. (1992a) Proc. Natl. Acad. Sci. USA 89:6988; Tuerk et al. (1992b) in Polymerase Chain Reaction (Ferre, F, Mullis, K., Gibbs, R. & Ross, A., eds.) Birkhauser, NY). Briefly, DNA templates for in vitro transcription (that contain a region of thirty random positions flanked by constant sequence regions) and the corresponding PCR primers were synthesized chemically (operon). The random region was generated by utilizing an equimolar mixture of the four nucleotides during oligonucleotide synthesis. The two constant regions were designed to contain PCR primer annealing sites, a primer annealing site for cDNA synthesis, T7 RNA polymerase promoter region, and restriction enzyme sites that allow cloning into vectors.

DEPR:
Four prototypic 5-modified uridines, 5-AA-UTP, 5-F-12-UTP, 5-Dig-11-UTP, and 5-Br-UTP (shown in FIG. 2) were incorporated into RNA by the T7 RNA polymerase under standard transcription conditions (40 mM Tris-Cl, pH 8.0, 12 mM MgCl.sub.2, 5 mM DTT, 1 mM spermidine, 0.002% Triton X-100, 4% PEG, 37.degree. C.). Autoradiogram of a 15% denaturing polyacrylamide gel showing products of transcription done with UTP, 5-AA-UTP, and 5-Br-UTP is shown in FIG. 3. The efficiency of transcription was estimated from the total amounts of .sup.32 p-radiolabelled transcript produced after three hours of incubation with 2 mM ribonucleotide triphosphates, 100 nM double-stranded DNA template, and 5 units/.mu.l of T7 RNA polymerase (NEB). 5-AA-UTP, 5-F-12-UTP, 5-Dig-11-UTP, and 5-Br-UTP were incorporated with 28%, 51%, 23%, and 50% efficiency, respectively, as compared to UTP. No transcription was detectable when UTP was omitted from the transcription mixture.

DEPR:
Modified transcripts containing 5-AA-UTP, 5-F-12-UTP, 5-Dig-11-UTP, or 5-Br-UTP were reverse transcribed into cDNA by AMV reverse transcriptase with efficiencies comparable to that of the unmodified RNA (done in 50 mM Tris, pH 8.3, 60 mM NaCl, 6 mM Mg(OAc).sub.2, 10 mM DTT, 37.degree. C.) (data not shown). These cDNAs were then amplified by PCR. Sequencing of the PCR products derived from UTP, 5-AA-UTP, and 5-Br-UTP transcriptions revealed that identical products were obtained in all three cases. These results show that modified nucleotides can be directly incorporated into the RNA SELEX procedure.

DEPR:
RNA was transcribed with T7 RNA polymerase from double-stranded DNA in a reaction containing ATP, GTP, 2'-NH.sub.2 -UTP, and 2'-NH.sub.2 -CTP.

DEPR:
Secondary structures were predicted for the high affinity 2'-OH and 2'-NH.sub.2 RNA ligands to thrombin shown in FIG. 7A-7F. Clone 17 is representative of the A subgroup of the group II 2'-NH.sub.2 ligands. Clone 16 is representative of the class I ligands of the 2'-OH ligands and clone 27 is representative of the class

II ligands of the 2'-OH ligands.

DEPR:
The synthesis of 2'-amino,2'-deoxy pyrimidine 5'-triphosphates has not previously been reported in full detail. The 2'-amino,2'-deoxyuridine 5'-triphosphate was prepared via 5'-phosphorylation of 2'-azido,2'-deoxyuridine and subsequent reduction (Aurup et al. (1992) supra). This route requires protection of the 3'-OH group, which can only be achieved selectively with intermittent protection of the 5'-OH group. Herein described is a method of preparing the compound in only two steps from 2'-amino,2'-deoxyuridine. The strategy relied on herein is based on the hypothesis that protection of the 3'-OH group is not necessary if the 2'-NH.sub.2 group carries a protecting group that blocks the 3'-OH during phosphorylation. The synthesis of 2'-amino,2'-deoxyuridine 5'-triphosphate herein described is shown in FIG. 10.

DEPR:
The 2'-amino group of 2'-amino,2'-deoxyuridine is trifluoroacetylated (Imazawa et al. (1979) J. Org. Chem. 44:2039) in 82% yield. This intermediate is phosphorylated at the 5'-position (Ludwig and Eckstein (1989) J. Org. Chem. 54:631) in 61% yield. The 5-iodo derivative of the 2'-amino,2'-deoxyuridine 5'-triphosphate was prepared by mercuration (Dale et al. (1975) supra) in a single step. Both 2'-amino,2'-deoxyuridine 5'-triphosphate and 5-iodo,2'-amino,2'-deoxyuridine 5'-triphosphate were shown to be substrates for T7 RNA polymerase. This has never been demonstrated before for the latter compound.

DEPR:
2'-(N-trifluoroacetyl)amino,2'-deoxyuridine (230 mg, 0.68 mmoles) was dried under vacuum for 3 h prior to dissolution in anhydrous dioxane (2 ml) and anhydrous pyridine (0.68 ml). To this solution was added a freshly prepared solution of 2-chloro-4H-1,3,2-benzodioxaphosphorin-4-one in anhydrous dioxane (152 mg, dissolved to 1M). The reaction was stirred at room temperature for 10 min prior to addition of a solution of bis(tri-n-butylammonium) pyrophosphate in anhydrous DMF (2.04 ml, 1.02 mmoles, 1.5 eq.) and tributylamine (162 .mu.l, 0.68 mmoles). After 15 min at room temperature an iodine solution was added (279 mg, 1% solution, pyridine/water 98:2 v/v). The mixture was stirred at room temperature for an additional 15 min and the excess iodine destroyed with aqueous NaHSCO.sub.4 (5% solution). The mixture was evaporated to dryness and the residue taken up in water (10 ml). After addition of concentrated ammonia (10 ml) the mixture set at room temperature for 1 h. The product was purified by DEAE Sephadex A25 (Pharmacia) chromatography (0-1 M triethylammonium bicarbonate buffer). To remove excess buffer salt, the product was repeatedly concentrated from methanol to yield 364 mg (62%) tetrakis (triethylammonium)-2'-amino,2'-deoxyuridine 5'-triphosphate. .sup.1 H NMR (300 MHz, methanol-d.sub.4) .delta. 7.21 (d, 1H, H.sub.6, J.sub.H6,H5 =8.1 Hz), 5.33 (d, 1H, H1', J.sub.H1',H2' =7.9 Hz), 5.05 (d, 1H,H.sub.5, J.sub.H6, H5 =8.1 Hz), 3.82 (dd, H.sub.3', JH.sub.3',H2' =5.3 Hz, J.sub.H3',H4' =1.6 Hz, 3.49 (m, 1H, HA), 3.42 (m, 1H, H.sub.4'), 3.38 (m, 1H, H.sub.5'.beta.), 3.08 (dd, 1H, H.sub.2', JH.sub.1',H2' =7.9 Hz, J.sub.H2',H.sub.3' =5.3 Hz), 2.52 (s, 1H, OH), 2.38 (q, 24H, --CH.sub.2), 0.52 (t, 36H, --CH.sub.3). .sup.31 P NMR (121.5 MHz, methanol-d.sub.4, H.sub.3 PO.sub.4 as external standard) .delta. -8.24 (d, P.sub..alpha., J.sub.P.gamma.P.beta. =21 Hz), -11.27 (d, P.sub..alpha., J.sub.P.alpha.,P.beta. =21 Hz), -22.43 (t, P.sub..beta., J=21Hz).

DEPR:
To a solution of tetrakis(triethylammonium)-2'-amino,2'-deoxyruidine 5'-triphosphate (35.2 mg, 0.02 mmoles, 0.02 M) in sodium acetate (0.1 M, 2 ml, pH 6.0) was added a solution of mercuric acetate (63.74 mg in 0.1 M sodium acetate, 0.01 M). The mixture was heated at 50.degree. C. for 3 h. After cooling to room temperature, a solution of iodine in ethanol (25.38 mg I.sub.2 in 80 .mu.l ethanol) was added. The mixture was stirred at room temperature in the dark for 1 h. The product was purified by DEAE Sephadex-A25 (Pharmacia) chromatography (0-1 M triethyl ammonium bicarbonate buffer). To remove excess buffer salt the product was repeatedly concentrated from methanol to yield 6 mg (30%) tetrakis(triethylammonium)-5-iodo,2'-amino,2'-deoxyuridine 5'-triphosphate. UV: .gamma.max 273 nm.

DEPL:
Secondary Structural Analysis.

partitioning unbound nucleic acids from those nucleic acids which have bound to target molecules, dissociating the nucleic acid-target pairs, amplifying the nucleic acids dissociated from the nucleic acid-target pairs to yield a ligand-enriched mixture of nucleic acids, then reiterating the steps of binding, partitioning, dissociating and amplifying through as many cycles as desired.

BSPR:
While not bound by theory, SELEX is based on the inventors' insight that within a nucleic acid mixture containing a large number of possible sequences and structures there is a wide range of binding affinities for a given target. A nucleic acid mixture comprising, for example a 20 nucleotide randomized segment can have 4.sup.20 candidate possibilities. Those which have the higher affinity constants for the target are most likely to bind to the target. After partitioning, dissociation and amplification, a second nucleic acid mixture is generated, enriched for the higher binding affinity candidates. Additional rounds of selection progressively favor the best ligands until the resulting nucleic acid mixture is predominantly composed of only one or a few sequences. These can then be cloned, sequenced and individually tested for binding affinity as pure ligands.

BSPR:
In many cases, it is not necessarily desirable to perform the iterative steps of SELEX until a single nucleic acid ligand is identified. The target-specific nucleic acid ligand solution may include a family of nucleic acid structures or motifs that have a number of conserved sequences and a number of sequences which can be substituted or added without significantly affecting the affinity of the nucleic acid ligands to the target. By terminating the SELEX process prior to completion, it is possible to determine the sequence of a number of members of the nucleic acid ligand solution family.

BSPR:
A variety of nucleic acid primary, secondary and tertiary structures are known to exist. The structures or motifs that have been shown most commonly to be involved in non-Watson-Crick type interactions are referred to as hairpin loops, symmetric and asymmetric bulges, pseudoknots and myriad combinations of the same. Almost all known cases of such motifs suggest that they can be formed in a nucleic acid sequence of no more than 30 nucleotides. For this reason, it is often preferred that SELEX procedures with contiguous randomized segments be initiated with nucleic acid sequences containing a randomized segment of between about 20-50 nucleotides.

BSPR:
The more prevailing mode of degradation of oligoribonucleotides proceeds through catalysis by endonucleases. Endonucleases cleave RNA within the chain, 3' to the specific base they recognize. The mechanism of cleavage involves activation of the 2'-hydroxyl (2'-OH) to attack the phosphorous of the internucleotidic linkage (Saenger (1984) in: Principles of Nucleic Acid Structure, Springer Verlag, N.Y., p. 174). This initial step leads to chain cleavage with formation of the 2',3'-cyclic phosphate end on the 5'-product and a free 5'-OH end on the 3'-product. The major degradation of oligoribonucleotides in serum proceeds through pyrimidine-specific endonuclease (Pieken et al. (1990) Science 253:314).

BSPR:
The resistance of 2'-amino,2'-deoxy pyrimidine homopolymers to degradation by pancreatic ribonuclease (RNAse A) has been reported. Both poly(2'-amino,2'-deoxyuridine) and poly(2'-amino,2'-deoxycytidine) are essentially completely stable towards RNAse A degradation. As expected, these polymers are readily degraded by snake venom phosphodiesterase, an enzyme that catalyzes water-hydrolysis of the phosphodiester backbone. The stability of 2'-amino,2'-deoxy pyrimidine containing oligonucleotides in rabbit serum is reported to be 1200-fold increased compared to unmodified oligoribonucleotides (Pieken et al. (1990) supra). This technology has been applied to the preparation of nuclease resistant hammerhead ribozymes (PCT Patent Application Publication WO 92/07065).

BSPR:
The stability of oligoribonucleotides against endonuclease degradation may be achieved by replacement of the 2'-OH group of the ribose moiety with an alternate substituent such as an amino group or a fluoro group (Pieken et al. (1991)

L8: Entry 8 of 52 File: USPT Feb 6, 2001

DOCUMENT-IDENTIFIER: US 6184364 B1
TITLE: High affinity nucleic acid ligands containing modified nucleotides

BSPR:
Most proteins or small molecules are not known to specifically bind to nucleic acids. The known protein exceptions are those regulatory proteins such as repressors, polymerases, activators and the like which function in a living cell to bring about the transfer of genetic information encoded in the nucleic acids into cellular structures and the replication of the genetic material. Furthermore, small molecules such as GTP bind to some intron RNAS.

BSPR:
Double-stranded RNA occasionally serves as a ligand for certain proteins, for example, the endonuclease RNase III from E. coli. There are more known instances of target proteins that bind to single-stranded RNA ligands, although in these cases the single-stranded RNA often forms a complex three-dimensional shape that includes local regions of intramolecular double-strandedness. The amino-acyl tRNA synthetases bind tightly to tRNA molecules with high specificity. A short region within the genomes of RNA viruses binds tightly and with high specificity to the viral coat proteins. A short sequence of RNA binds to the bacteriophage T4-encoded DNA polymerase, again with high affinity and specificity. Thus, it is possible to find RNA and DNA ligands, either double- or single-stranded, serving as binding partners for specific protein targets. Most known DNA binding proteins bind specifically to double-stranded DNA, while most RNA binding proteins recognize single-stranded RNA. This statistical bias in the literature no doubt reflects the present biosphere's statistical predisposition to use DNA as a double-stranded genome and RNA as a single-stranded entity in the roles RNA plays beyond serving as a genome. Chemically there is no strong reason to dismiss single-stranded DNA as a fully able partner for specific protein interactions.

BSPR:.
RNA and DNA have also been found to bind to smaller target molecules. Double-stranded DNA binds to various antibiotics, such as actinomycin D. A specific single-stranded RNA binds to the antibiotic thiostreptone; specific RNA sequences and structures probably bind to certain other antibiotics, especially those whose function is to inactivate ribosomes in a target organism. A family of evolutionary related RNAs binds with specificity and decent affinity to nucleotides and nucleosides (Bass, B. and Cech, T. (1984) Nature 308:820-826) as well as to one of the twenty amino acids (Yarus, M. (1988) Science 240:1751-1758). Catalytic RNAs are now known as well, although these molecules perform over a narrow range of chemical possibilities, which are thus far related largely to phosphodiester transfer reactions and hydrolysis of nucleic acids.

BSPR:
Despite these known instances, the great majority of proteins and other cellular components are thought not to bind to nucleic acids under physiological conditions and such binding as may be observed is non-specific. Either the capacity of nucleic acids to bind other compounds is limited to the relatively few instances enumerated supra, or the chemical repertoire of the nucleic acids for specific binding is avoided (selected against) in the structures that occur naturally. The present invention is premised on the inventors' fundamental insight that nucleic acids as chemical compounds can form a virtually limitless array of shapes, sizes and configurations, and are capable of a far broader repertoire of binding and catalytic functions than those displayed in biological systems.

BSPR:
The chemical interactions have been explored in cases of certain known instances of protein-nucleic acid binding. For example, the size and sequence of the RNA site of bacteriophage R17 coat protein binding has been identified by Uhlenbeck and coworkers. The minimal natural RNA binding site (21 bases long) for the R17 coat protein was determined by subjecting variable-sized labeled fragments of the mRNA to nitrocellulose filter binding assays in which protein-RNA fragment complexes remain bound to the filter (Carey et al. (1983) Biochemistry 22:2601). A number of sequence variants of the minimal R17 coat protein binding site were created in vitro in order to determine the contributions of individual nucleic acids to protein binding (Uhlenbeck et al. (1983) J. Biomol. Structure and Dynamics 1:539 and Romaniuk et al. (1987) Biochemistry 26:1563). It was found that the maintenance of the hairpin loop structure of the binding site was essential for protein binding but, in addition, that nucleotide substitutions at most of the single-stranded residues in the binding site, including a bulged nucleotide in the hairpin stem, significantly affected binding. In similar studies, the binding of bacteriophage Q.beta. coat protein to its translational operator was examined (Witherell and Uhlenbeck (1989) Biochemistry 28:71). The Q.beta. coat protein RNA binding site was found to be similar to that of R17 in size, and in predicted secondary structure, in that it comprised about 20 bases with an 8 base pair hairpin structure which included a bulged nucleotide and a 3 base loop. In contrast to the R17 coat protein binding site, only one of the single-stranded residues of the loop is essential for binding and the presence of the bulged nucleotide is not required. The protein-RNA binding interactions involved in translational regulation display significant specificity.

BSPR:
Nucleic acids are known to form secondary and tertiary structures in solution. The double-stranded forms of DNA include the so-called B double-helical form, Z-DNA and superhelical twists (Rich, A. et al. (1984) Ann. Rev. Biochem. 53:791-846). Single-stranded RNA forms localized regions of secondary structure such as hairpin loops and pseudoknot structures (Schimmel, P. (1989) Cell 58:9-12). However, little is known concerning the effects of unpaired loop nucleotides on stability of loop structure, kinetics of formation and denaturation, thermodynamics, and almost nothing is known of tertiary structures and three dimensional shape, nor of the kinetics and thermodynamics of tertiary folding in nucleic acids (Tuerk, C. et al. (1988) Proc. Natl. Acad. Sci. USA 85:1364-1368).

BSPR:
Joyce and Robertson (Joyce (1989) in RNA: Catalysis, Splicing. Evolution, Belfort and Shub (eds.), Elsevier, Amsterdam pp. 83-87; and Robertson and Joyce (1990) Nature 344:467) reported a method for identifying RNAs which specifically cleave single-stranded DNA. The selection for catalytic activity was based on the ability of the ribozyme to catalyze the cleavage of a substrate ssRNA or DNA at a specific position and transfer the 3'-end of the substrate to the 3'-end of the ribozyme. The product of the desired reaction was selected by using a deoxyoligonucleotide primer which could bind only to the completed product across the junction formed by the catalytic reaction and allowed selective reverse transcription of the ribozyme sequence. The selected catalytic sequences were amplified by attachment of the promoter of T7 RNA polymerase to the 3'-end of the cDNA, followed by transcription to RNA. The method was employed to identify from a small number of ribozyme variants the variant that was most reactive for cleavage of a selected substrate.

BSPR:
The method of the SELEX Patent Applications is based on the unique insight that nucleic acids have sufficient capacity for forming a variety of two- and three-dimensional structures and sufficient chemical versatility available within their monomers to act as ligands (form specific binding pairs) with virtually any chemical compound, whether large or small in size.

BSPR:
The method involves selection from a mixture of candidates and step-wise iterations of structural improvement, using the same general selection theme, to achieve virtually any desired criterion of binding affinity and selectivity. Starting from a mixture of nucleic acids, preferably comprising a segment of randomized sequence, the method, termed SELEX herein, includes steps of contacting the mixture with the target under conditions favorable for binding,

DEPL:
2'-Amino, 2'-deoxyuridine 5'-triphosphate.

DEPL:
5'Iodo, 2'-amino,2'-deoxyuridine 5'-triphosphate.

DEPC:
Synthesis of 5-iodo,2'-amino,2'-deoxy pyrimidine 5'-triphosphates.

CLPR:
2. A method of preparing 5-iodo,2'-amino,2'-deoxy uridine 5'-triphosphate from 2'-amino,2'-deoxyuridine, comprising:

CLPV:
b) phosphorylating 2'-trifluoroacetylamino,2'-deoxyuridine to 2'-amino,2'-deoxyuridine 5'-triphosphate; and

CLPV:
c) iodinating 2'-trifluoroacetylamino,2'-deoxyuridine by mercuration to form 5'-iodo,2'-amino,2'-deoxyuridine 5'-triphosphate.

ORPL:
Szostak, "Structure and Activity of Ribozymes," in Redesigning the Molecules of Life, (S.A. Benner ed.) Springer-Verlag Berline Heidelberg, pp. 87-113 (1988).

ORPL:
Verheyden et al. "Synthesis of some pyrimidine 2'-amino-2-deoxynucleosides" J. Org. Chem. vol. 36, No. 2, 1971.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 8. Document ID: US 6184364 B1

L7: Entry 8 of 52 File: USPT Feb 6, 2001

US-PAT-NO: 6184364
DOCUMENT-IDENTIFIER: US 6184364 B1

TITLE: High affinity nucleic acid ligands containing modified nucleotides

DATE-ISSUED: February 6, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Kirschenheuter; Gary P	Arvada	CO	N/A	N/A

US-CL-CURRENT: 536/4.1; 435/6, 536/22.1, 536/28.1, 536/28.2, 536/28.3, 536/28.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 9. Document ID: US 6180352 B1

L7: Entry 9 of 52 File: USPT Jan 30, 2001

US-PAT-NO: 6180352
DOCUMENT-IDENTIFIER: US 6180352 B1

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: January 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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US-CL-CURRENT: 435/6; 536/23.1, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 10. Document ID: US 6177250 B1

L7: Entry 10 of 52 File: USPT Jan 23, 2001

US-PAT-NO: 6177250
DOCUMENT-IDENTIFIER: US 6177250 B1

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

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Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	La Canada-Flintridge	CA	N/A	N/A

US-CL-CURRENT: 435/6; 536/23.1, 536/24.3

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☐ 11. Document ID: US 6150510 A

L7: Entry 11 of 52 File: USPT Nov 21, 2000

US-PAT-NO: 6150510
DOCUMENT-IDENTIFIER: US 6150510 A

TITLE: Modified oligonucleotides, their preparation and their use

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seela; Frank	Osnabruck	N/A	N/A	DEX
Thomas; Horst	Hasbergen	N/A	N/A	DEX

US-CL-CURRENT: 536/22.1; 435/6, 435/91.1, 435/91.2, 536/23.1, 536/24.1, 536/24.3, 536/24.5, 536/25.3, 536/25.6, 536/27.1 , 536/27.11, 536/27.13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 12. Document ID: US 6143715 A

L7: Entry 12 of 52 File: USPT Nov 7, 2000

US-PAT-NO: 6143715
DOCUMENT-IDENTIFIER: US 6143715 A

TITLE: Hepatitis C inhibitor peptide analogues

DATE-ISSUED: November 7, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Llinas-Brunet; Montse	Pierrefonds	N/A	N/A	CAX
Bailey; Murray D.	Pierrefonds	N/A	N/A	CAX
Halmos; Teddy	Laval	N/A	N/A	CAX
Poupart; Marc-Andre	Laval	N/A	N/A	CAX
Tsantrizos; Youla	Saint-Laurent	N/A	N/A	CAX

US-CL-CURRENT: 514/2; 424/189.1, 514/17, 514/18, 530/329, 530/330

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 13. Document ID: US 6140053 A

L7: Entry 13 of 52 File: USPT Oct 31, 2000

US-PAT-NO: 6140053
DOCUMENT-IDENTIFIER: US 6140053 A

TITLE: DNA sequencing by mass spectrometry via exonuclease degradation

DATE-ISSUED: October 31, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 435/6; 422/68.1, 536/25.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 14. Document ID: US 6140051 A

L7: Entry 14 of 52 File: USPT Oct 31, 2000

US-PAT-NO: 6140051
DOCUMENT-IDENTIFIER: US 6140051 A

TITLE: Fluorescent dibenzazole derivatives and methods related thereto

DATE-ISSUED: October 31, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brown; Lauren R.	San Luis Obispo	CA	N/A	N/A
Xu; Cheng	San Mateo	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 435/7.2, 436/501, 548/100, 548/122, 548/215, 548/217, 548/219, 548/335.1, 548/400, 548/407, 548/416

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 15. Document ID: US 6127535 A

L7: Entry 15 of 52 File: USPT Oct 3, 2000

US-PAT-NO: 6127535
DOCUMENT-IDENTIFIER: US 6127535 A

TITLE: Nucleoside triphosphates and their incorporation into oligonucleotides

DATE-ISSUED: October 3, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Beigelman; Leonid	Longmont	CO	N/A	N/A
Burgin; Alex	Chula Vista	CA	N/A	N/A
Beaudry; Amber	Broomfield	CO	N/A	N/A
Karpeisky; Alexander	Lafayette	CO	N/A	N/A
Matulic-Adamic; Jasenka	Boulder	CO	N/A	N/A
Sweedler; David	Louisville	CO	N/A	N/A

US-CL-CURRENT: 536/26.26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

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☐ 16. Document ID: US 6110462 A

L7: Entry 16 of 52 File: USPT Aug 29, 2000

US-PAT-NO: 6110462
DOCUMENT-IDENTIFIER: US 6110462 A

TITLE: Enzymatic DNA molecules that contain modified nucleotides

DATE-ISSUED: August 29, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Barbas; Carlos F.	Del Mar	CA	N/A	N/A
Joyce; Gerald	Encinitas	CA	N/A	N/A
Santoro; Stephen W.	San Diego	CA	N/A	N/A
Kandasamy; Sakthivel	San Diego	CA	N/A	N/A

US-CL-CURRENT: 424/94.6; 424/94.1, 424/94.61, 435/183, 435/196, 435/199, 435/91.1, 435/91.31, 435/91.53, 536/23.1, 536/24.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

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☐ 17. Document ID: US 6107039 A

L7: Entry 17 of 52 File: USPT Aug 22, 2000

US-PAT-NO: 6107039
DOCUMENT-IDENTIFIER: US 6107039 A

TITLE: Assays using base protected table 1

DATE-ISSUED: August 22, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hanna; Michelle M.	Norman	OK	N/A	N/A

US-CL-CURRENT: 435/6; 536/23.1, 536/25.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 18. Document ID: US 6096273 A

L7: Entry 18 of 52 File: USPT Aug 1, 2000

US-PAT-NO: 6096273
DOCUMENT-IDENTIFIER: US 6096273 A

TITLE: Electrodes linked via conductive oligomers to nucleic acids

DATE-ISSUED: August 1, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kayyem; Jon F.	Pasadena	CA	N/A	N/A
O'Connor; Stephen D.	Pasadena	CA	N/A	N/A
Gozin; Michael	Pasadena	CA	N/A	N/A
Yu; Changjun	Pasadena	CA	N/A	N/A
Meade; Thomas J.	Altadena	CA	N/A	N/A

US-CL-CURRENT: 422/68.1; 435/283.1, 435/6, 436/501, 536/22.1, 536/25.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 19. Document ID: US 6090933 A

L7: Entry 19 of 52 File: USPT Jul 18, 2000

US-PAT-NO: 6090933
DOCUMENT-IDENTIFIER: US 6090933 A

TITLE: Methods of attaching conductive oligomers to electrodes

DATE-ISSUED: July 18, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
O'Connor; Stephen D.	Pasadena	CA	N/A	N/A
Gozin; Michael	Beer Sheva	N/A	N/A	ILX
Yu; Changjun	Pasadena	CA	N/A	N/A
Meade; Thomas J.	Altadena	CA	N/A	N/A

US-CL-CURRENT: 536/25.3; 422/50, 422/68.1, 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 20. Document ID: US 6087100 A

L7: Entry 20 of 52 File: USPT Jul 11, 2000

US-PAT-NO: 6087100
DOCUMENT-IDENTIFIER: US 6087100 A

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: July 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	Newport Beach	CA	N/A	N/A

US-CL-CURRENT: 435/6; 536/23.1, 536/24.2, 536/24.3, 536/24.31

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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Term	Documents
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☐ 21. Document ID: US 6074823 A

L7: Entry 21 of 52 File: USPT Jun 13, 2000

US-PAT-NO: 6074823
DOCUMENT-IDENTIFIER: US 6074823 A

TITLE: DNA sequencing by mass spectrometry via exonuclease degradation

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 435/6; 250/282, 435/196

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 22. Document ID: US 6071699 A

L7: Entry 22 of 52 File: USPT Jun 6, 2000

US-PAT-NO: 6071699
DOCUMENT-IDENTIFIER: US 6071699 A

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: June 6, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	Newport Beach	CA	N/A	N/A

US-CL-CURRENT: 435/6; 436/149, 436/2, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 23. Document ID: US 6066720 A

L7: Entry 23 of 52 File: USPT May 23, 2000

US-PAT-NO: 6066720
DOCUMENT-IDENTIFIER: US 6066720 A

TITLE: Modified oligonucleotides, their preparation and their use

DATE-ISSUED: May 23, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seela; Frank	Osnabruck	N/A	N/A	DEX
Lampe; Sigrid	Berge/Hekese	N/A	N/A	DEX

US-CL-CURRENT: 536/22.1; 435/6, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/25.3, 536/25.32, 536/27.1, 536/27.11, 536/27.12, 536/27.13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 24. Document ID: US 6028183 A

L7: Entry 24 of 52 File: USPT Feb 22, 2000

US-PAT-NO: 6028183
DOCUMENT-IDENTIFIER: US 6028183 A

TITLE: Pyrimidine derivatives and oligonucleotides containing same

DATE-ISSUED: February 22, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lin; Kuei-Ying	Fremont	CA	N/A	N/A
Matteucci; Mark D.	Portola Valley	CA	N/A	N/A

US-CL-CURRENT: 536/22.1; 435/6, 435/87, 435/90, 536/23.1, 536/25.3, 536/25.31, 536/25.32, 536/25.34, 536/25.4, 544/249

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 25. Document ID: US 6008334 A

L7: Entry 25 of 52 File: USPT Dec 28, 1999

US-PAT-NO: 6008334
DOCUMENT-IDENTIFIER: US 6008334 A

TITLE: Base-protected nucleotide analogs with protected thiol groups

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hanna; Michelle M.	Norman	OK	N/A	N/A

US-CL-CURRENT: 536/22.1; 435/6, 436/501, 536/23.1, 536/24.1, 536/24.3, 536/24.31, 536/24.32, 536/24.33, 536/25.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 26. Document ID: US 6007992 A

L7: Entry 26 of 52 File: USPT Dec 28, 1999

US-PAT-NO: 6007992
DOCUMENT-IDENTIFIER: US 6007992 A

TITLE: Pyrimidine derivatives for labeled binding partners

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lin; Kuei-Ying	Fremont	CA	N/A	N/A
Matteucci; Mark D.	Portola Valley	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/87, 435/90, 435/91.1, 536/22.1, 536/23.1, 536/25.3, 536/25.31, 536/25.32, 536/25.34, 536/25.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 27. Document ID: US 6005096 A

L7: Entry 27 of 52 File: USPT Dec 21, 1999

US-PAT-NO: 6005096
DOCUMENT-IDENTIFIER: US 6005096 A

TITLE: Pyrimidine derivatives

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Matteucci; Mark	Burlingame	CA	N/A	N/A
Jones; Robert J.	Millbrae	CA	N/A	N/A
Lin; Kuei-Ying	Fremont	CA	N/A	N/A

US-CL-CURRENT: 536/26.6; 544/300, 544/316, 544/317, 544/318

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 28. Document ID: US 5952172 A

L7: Entry 28 of 52 File: USPT Sep 14, 1999

US-PAT-NO: 5952172
DOCUMENT-IDENTIFIER: US 5952172 A

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: September 14, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	La Canada	CA	N/A	N/A

US-CL-CURRENT: 435/6; 536/24.3, 536/24.31, 536/24.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 29. Document ID: US 5939262 A

L7: Entry 29 of 52 File: USPT Aug 17, 1999

US-PAT-NO: 5939262
DOCUMENT-IDENTIFIER: US 5939262 A

TITLE: Ribonuclease resistant RNA preparation and utilization

DATE-ISSUED: August 17, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pasloske; Brittan L.	Austin	TX	N/A	N/A
DuBois; Dwight	Austin	TX	N/A	N/A
Brown; David	Austin	TX	N/A	N/A
Winkler; Matthew	Austin	TX	N/A	N/A

US-CL-CURRENT: 435/6; 435/235.1, 536/23.1, 536/24.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 30. Document ID: US 5872003 A

L7: Entry 30 of 52 File: USPT Feb 16, 1999

US-PAT-NO: 5872003
DOCUMENT-IDENTIFIER: US 5872003 A

TITLE: DNA sequencing by mass spectrometry via exonuclease degradation

DATE-ISSUED: February 16, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 435/283.1; 435/286.1, 435/287.2, 435/287.3, 435/288.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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Term	Documents
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TRIPHOSPHAT.DWPI,EPAB,JPAB,USPT,PGPB.	45
TRIPHOSPHATAS.DWPI,EPAB,JPAB,USPT,PGPB.	1
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TRIPHOSPHATEIS.DWPI,EPAB,JPAB,USPT,PGPB.	1
TRIPHOSPHATEOR.DWPI,EPAB,JPAB,USPT,PGPB.	2
TRIPHOSPHATES.DWPI,EPAB,JPAB,USPT,PGPB.	4993
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☐ 31. Document ID: US 5861493 A

L7: Entry 31 of 52 File: USPT Jan 19, 1999

US-PAT-NO: 5861493
DOCUMENT-IDENTIFIER: US 5861493 A

TITLE: Process for the synthesis of 2'-O-substituted pyrimidines

DATE-ISSUED: January 19, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cook; Phillip Dan	San Marcos	CA	N/A	N/A
Springer; Robert H.	Carlsbad	CA	N/A	N/A
Sprankle; Kelly G.	Vista	CA	N/A	N/A
Ross; Bruce S.	Carlsbad	CA	N/A	N/A

US-CL-CURRENT: 536/22.1; 536/23.1, 536/25.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 32. Document ID: US 5856085 A

L7: Entry 32 of 52 File: USPT Jan 5, 1999

US-PAT-NO: 5856085
DOCUMENT-IDENTIFIER: US 5856085 A

TITLE: Compositions and methods of developing oligonucleotides and oligonucleotide analogs having antiviral activity

DATE-ISSUED: January 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wang; Jin-Feng	Hummelstown	PA	N/A	N/A
Pan; Weihua	Hershey	PA	N/A	N/A

US-CL-CURRENT: 435/5; 435/6, 435/91.2, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 33. Document ID: US 5851765 A

L7: Entry 33 of 52 File: USPT Dec 22, 1998

US-PAT-NO: 5851765
DOCUMENT-IDENTIFIER: US 5851765 A

TITLE: DNA sequencing by mass spectrometry via exonuclease degradation

DATE-ISSUED: December 22, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 435/6; 250/281, 250/282, 435/91.2, 536/22.1, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 34. Document ID: US 5846720 A

L7: Entry 34 of 52 File: USPT Dec 8, 1998

US-PAT-NO: 5846720
DOCUMENT-IDENTIFIER: US 5846720 A

TITLE: Methods of determining chemicals that modulate expression of genes associated with cardiovascular disease

DATE-ISSUED: December 8, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Foulkes; J. Gordon	Huntington Station	NY	N/A	N/A
Liechtfried; Franz E.	Vienna	N/A	N/A	ATX
Pieler; Christian	Vienna	N/A	N/A	ATX
Stephenson; John R.	Santa Cruz	CA	N/A	N/A
Case; Casey C.	Lynbrook	NY	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/69.8, 435/91.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 35. Document ID: US 5844106 A

L7: Entry 35 of 52 File: USPT Dec 1, 1998

US-PAT-NO: 5844106
DOCUMENT-IDENTIFIER: US 5844106 A

TITLE: Modified oligonucleotides, their preparation and their use

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seela; Frank	Osnabrueck	N/A	N/A	DEX
Thomas; Horst	Hasbergen	N/A	N/A	DEX

US-CL-CURRENT: 536/22.1; 536/23.1, 536/24.3, 536/25.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 36. Document ID: US 5830653 A

L7: Entry 36 of 52 File: USPT Nov 3, 1998

US-PAT-NO: 5830653
DOCUMENT-IDENTIFIER: US 5830653 A

TITLE: Methods of using oligomers containing modified pyrimidines

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Froehler; Brian	Belmont	CA	N/A	N/A
Wagner; Rick	Belmont	CA	N/A	N/A
Matteucci; Mark	Burlingame	CA	N/A	N/A
Jones; Robert J.	Millbrae	CA	N/A	N/A
Gutierrez; Arnold J.	San Jose	CA	N/A	N/A
Pudlo; Jeff	Burlingame	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/325, 435/375, 514/44, 536/24.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 37. Document ID: US 5824473 A

L7: Entry 37 of 52 File: USPT Oct 20, 1998

US-PAT-NO: 5824473
DOCUMENT-IDENTIFIER: US 5824473 A

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	Newport Beach	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/5, 435/91.2, 536/23.1, 536/24.3, 536/24.33, 536/26.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 38. Document ID: US 5789562 A

L7: Entry 38 of 52 File: USPT Aug 4, 1998

US-PAT-NO: 5789562
DOCUMENT-IDENTIFIER: US 5789562 A

TITLE: Nucleotide monomers containing 8-azapurin bases or a derivative thereof, their preparation and their use in making modified oligonucleotides

DATE-ISSUED: August 4, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seela; Frank	Osnabruck	N/A	N/A	DEX
Lampe; Sigrid	Berge/Hekese	N/A	N/A	DEX

US-CL-CURRENT: 536/22.1; 435/6, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 39. Document ID: US 5780234 A

L7: Entry 39 of 52 File: USPT Jul 14, 1998

US-PAT-NO: 5780234
DOCUMENT-IDENTIFIER: US 5780234 A

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: July 14, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	Newport Beach	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/5, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.32, 536/24.33, 536/26.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 40. Document ID: US 5770369 A

L7: Entry 40 of 52 File: USPT Jun 23, 1998

US-PAT-NO: 5770369
DOCUMENT-IDENTIFIER: US 5770369 A

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	Newport Beach	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/287.2, 435/5, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.33, 536/25.3, 536/26.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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TRIPHOSPHATEOR.DWPI,EPAB,JPAB,USPT,PGPB.	2
TRIPHOSPHATES.DWPI,EPAB,JPAB,USPT,PGPB.	4993
(L6 AND (TRIPHOSPHAT$3)).USPT,PGPB,JPAB,EPAB,DWPI.	52

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Display 10 Documents, starting with Document: 41

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Search Results - Record(s) 41 through 50 of 52 returned.

☐ 41. Document ID: US 5763588 A

L7: Entry 41 of 52 File: USPT Jun 9, 1998

US-PAT-NO: 5763588
DOCUMENT-IDENTIFIER: US 5763588 A

TITLE: Pyrimidine derivatives for labeled binding partners

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Matteucci; Mark D.	Burlingame	CA	N/A	N/A
Jones; Robert J.	Millbrae	CA	N/A	N/A

US-CL-CURRENT: 536/22.1; 534/768, 536/26.1, 536/26.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 42. Document ID: US 5763208 A

L7: Entry 42 of 52 File: USPT Jun 9, 1998

US-PAT-NO: 5763208
DOCUMENT-IDENTIFIER: US 5763208 A

TITLE: Oligonucleotides and their analogs capable of passive cell membrane permeation

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bischofberger; Norbert	San Carlos	CA	N/A	N/A
Kent; Ken	Mountain View	CA	N/A	N/A
Wagner; Rick	Burlingame	CA	N/A	N/A
Buhr; Chris	Daly City	CA	N/A	N/A
Lin; Kuei-Ying	Fremont	CA	N/A	N/A

US-CL-CURRENT: 435/40.5; 536/22.1, 536/24.3, 536/24.31, 536/24.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 43. Document ID: US 5705348 A

L7: Entry 43 of 52 File: USPT Jan 6, 1998

US-PAT-NO: 5705348
DOCUMENT-IDENTIFIER: US 5705348 A

TITLE: Nucleic acid mediated electron transfer

DATE-ISSUED: January 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meade; Thomas J.	Altadena	CA	N/A	N/A
Kayyem; Jon Faiz	Pasadena	CA	N/A	N/A
Fraser; Scott E.	Newport Beach	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/5, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.32, 536/24.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

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☐ 44. Document ID: US 5702884 A

L7: Entry 44 of 52 File: USPT Dec 30, 1997

US-PAT-NO: 5702884
DOCUMENT-IDENTIFIER: US 5702884 A

TITLE: Whole blood sample preparation for polymerase chain reaction using ammonium chloride and a carboxylic acid or metal carboxylate for selective red blood cell lysis

DATE-ISSUED: December 30, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ekeze; Tobias E.	Brockport	NY	N/A	N/A
Kerschner; JoAnne Hansen	Rochester	NY	N/A	N/A

US-CL-CURRENT: 435/5; 424/534, 435/6, 435/91.2, 536/24.3, 536/24.32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

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☐ 45. Document ID: US 5691141 A

L7: Entry 45 of 52 File: USPT Nov 25, 1997

US-PAT-NO: 5691141
DOCUMENT-IDENTIFIER: US 5691141 A

TITLE: DNA sequencing by mass spectrometry

DATE-ISSUED: November 25, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/810, 435/91.1, 436/173, 436/174, 536/24.33, 536/25.3, 536/25.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 46. Document ID: US 5645985 A

L7: Entry 46 of 52 File: USPT Jul 8, 1997

US-PAT-NO: 5645985
DOCUMENT-IDENTIFIER: US 5645985 A

TITLE: Enhanced triple-helix and double-helix formation with oligomers containing modified pyrimidines

DATE-ISSUED: July 8, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Froehler; Brian	Belmont	CA	N/A	N/A
Wagner; Rick	Belmont	CA	N/A	N/A
Matteucci; Mark	Burlingame	CA	N/A	N/A
Jones; Robert J.	Millbrae	CA	N/A	N/A
Gutierrez; Arnold J.	Sandy Lane	CA	N/A	N/A
Pudlo; Jeff	Burlingame	CA	N/A	N/A

US-CL-CURRENT: 435/6; 536/24.3, 536/24.31, 536/24.32, 536/24.5, 536/26.8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 47. Document ID: US 5622824 A

L7: Entry 47 of 52 File: USPT Apr 22, 1997

US-PAT-NO: 5622824
DOCUMENT-IDENTIFIER: US 5622824 A

TITLE: DNA sequencing by mass spectrometry via exonuclease degradation

DATE-ISSUED: April 22, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
K oster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 435/6; 250/282, 250/288, 422/68.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 48. Document ID: US 5604207 A

L7: Entry 48 of 52 File: USPT Feb 18, 1997

US-PAT-NO: 5604207
DOCUMENT-IDENTIFIER: US 5604207 A

TITLE: Sialyl Le.sup.x analogues as inhibitors of cellular adhesion

DATE-ISSUED: February 18, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
DeFrees; Shawn A.	San Marcos	CA	N/A	N/A
Gaeta; Federico C. A.	Olivenhain	CA	N/A	N/A
Gaudino; John J.	Westlake Village	CA	N/A	N/A
Zheng; Zhongli	Lexington	MA	N/A	N/A
Hayashi; Masaji	Kobe	N/A	N/A	JPX

US-CL-CURRENT: 514/25; 514/54, 514/61, 514/62, 536/17.2, 536/55, 536/55.1, 536/55.2, 536/63, 536/64, 536/65

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 49. Document ID: US 5580722 A

L7: Entry 49 of 52 File: USPT Dec 3, 1996

US-PAT-NO: 5580722
DOCUMENT-IDENTIFIER: US 5580722 A

TITLE: Methods of determining chemicals that modulate transcriptionally expression of genes associated with cardiovascular disease

DATE-ISSUED: December 3, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Foulkes; J. Gordon	Huntington Station	NY	N/A	N/A
Liechtfried; Franz E.	Vienna	N/A	N/A	ATX
Pieler; Christian	Vienna	N/A	N/A	ATX
Stephenson; John R.	Santa Cruz	CA	N/A	N/A
Case; Casey C.	Lynbrook	NY	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.1, 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 50. Document ID: US 5547835 A

L7: Entry 50 of 52 File: USPT Aug 20, 1996

US-PAT-NO: 5547835
DOCUMENT-IDENTIFIER: US 5547835 A

TITLE: DNA sequencing by mass spectrometry

DATE-ISSUED: August 20, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Koster; Hubert	Concord	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/287.2, 435/288.7, 435/91.1, 436/173, 436/94, 536/25.3, 536/25.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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Term	Documents
TRIPHOSPHAT$3	0
TRIPHOSPHAT.DWPI,EPAB,JPAB,USPT,PGPB.	45
TRIPHOSPHATAS.DWPI,EPAB,JPAB,USPT,PGPB.	1
TRIPHOSPHATASE.DWPI,EPAB,JPAB,USPT,PGPB.	273
TRIPHOSPHATE.DWPI,EPAB,JPAB,USPT,PGPB.	10226
TRIPHOSPHATEA.DWPI,EPAB,JPAB,USPT,PGPB.	1
TRIPHOSPHATED.DWPI,EPAB,JPAB,USPT,PGPB.	5
TRIPHOSPHATEIS.DWPI,EPAB,JPAB,USPT,PGPB.	1
TRIPHOSPHATEOR.DWPI,EPAB,JPAB,USPT,PGPB.	2
TRIPHOSPHATES.DWPI,EPAB,JPAB,USPT,PGPB.	4993
(L6 AND (TRIPHOSPHAT$3)).USPT,PGPB,JPAB,EPAB,DWPI.	52

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☐ 51. Document ID: US 5502177 A

L7: Entry 51 of 52 File: USPT Mar 26, 1996

US-PAT-NO: 5502177
DOCUMENT-IDENTIFIER: US 5502177 A

TITLE: Pyrimidine derivatives for labeled binding partners

DATE-ISSUED: March 26, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Matteucci; Mark D.	Burlingame	CA	N/A	N/A
Jones; Robert J.	Millbrae	CA	N/A	N/A
Lin; Kuei-Ying	Fremont	CA	N/A	N/A

US-CL-CURRENT: 536/26.6; 544/102, 544/103

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 52. Document ID: US 5472841 A

L7: Entry 52 of 52 File: USPT Dec 5, 1995

US-PAT-NO: 5472841
DOCUMENT-IDENTIFIER: US 5472841 A

TITLE: Methods for identifying nucleic acid ligands of human neutrophil elastase

DATE-ISSUED: December 5, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jayasena; Sumedha D.	Boulder	CO	N/A	N/A
Gold; Larry	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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Term	Documents
TRIPHOSPHAT$3	0
TRIPHOSPHAT.DWPI,EPAB,JPAB,USPT,PGPB.	45
TRIPHOSPHATAS.DWPI,EPAB,JPAB,USPT,PGPB.	1
TRIPHOSPHATASE.DWPI,EPAB,JPAB,USPT,PGPB.	273
TRIPHOSPHATE.DWPI,EPAB,JPAB,USPT,PGPB.	10226
TRIPHOSPHATEA.DWPI,EPAB,JPAB,USPT,PGPB.	1
TRIPHOSPHATED.DWPI,EPAB,JPAB,USPT,PGPB.	5
TRIPHOSPHATEIS.DWPI,EPAB,JPAB,USPT,PGPB.	1
TRIPHOSPHATEOR.DWPI,EPAB,JPAB,USPT,PGPB.	2
TRIPHOSPHATES.DWPI,EPAB,JPAB,USPT,PGPB.	4993
(L6 AND (TRIPHOSPHAT$3)).USPT,PGPB,JPAB,EPAB,DWPI.	52

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